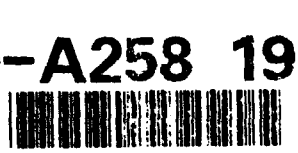


1992 THESIS/~~EXSSERXXXXEN~~

Relation Between Cigarette Smoking, Body Fat Distribution and Density of Lipoprotein Cholesterol in Women

Linda R. Beson, Major

AFIT Student Attending: University of Florida

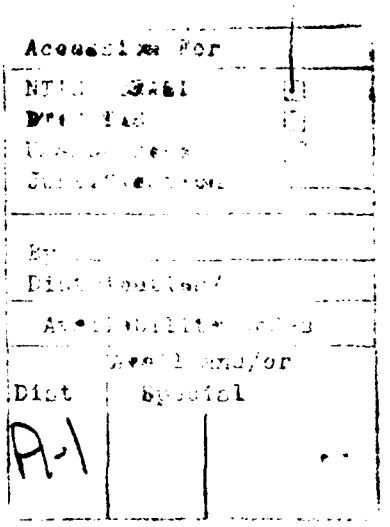
AFIT/CI/CIA-92-085

AFIT/CI
Wright-Patterson AFB OH 45433-6583

RELATION BETWEEN CIGARETTE SMOKING, BODY FAT DISTRIBUTION AND DENSITY OF LIPOPROTEIN CHOLESTEROL IN WOMEN

By

LINDA R. BESON



A THESIS PRESENTED TO THE GRADUATE SCHOOL
OF THE UNIVERSITY OF FLORIDA IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF
MASTER OF SCIENCE IN NURSING

UNIVERSITY OF FLORIDA

1992

ACKNOWLEDGEMENTS

I would like to acknowledge the many people who graciously helped make this research possible. First, I would like to thank my committee chairperson Dr. Sandra Seymour for her understanding and support, and for her guidance in overcoming the many obstacles encountered during this project. To Mary Ann House-Fancher, I extend my sincere thanks for her contagious enthusiasm, her willingness to share her expertise in cardiovascular nursing, and her assistance with data collection. I would also like to thank Dr. Hossein Yarandi, for his patience and assistance with the statistical analysis.

Very special thanks are extended to all those individuals at MacDill Air Force Base who were instrumental in providing the crucial laboratory support that made this study feasible: Lieutenant Colonel Mary Ann Cardinali, Assistant Chief Nurse, for her interest and support of nursing research; Lieutenant Colonel Sherrell L. Russell, Chief, Laboratory Services, for her delightful sense of humor and willingness to help; Sergeant Ciballos for his assistance with the proposal approval process; and all the laboratory personnel who assisted in processing the lipid profiles.

I would also like to thank the individuals who were instrumental in securing the sites for data collection and in recruiting volunteers: Dawn O'Byrne, MS, RD, for graciously sharing her data; Dr. Carolyn Reins and others at the Alachua County Health Department; Kay Nichols and Joe Ciruli at the Gainesville Health and Fitness Center; and Nancy Rodriguez and Lynn Burnsed at the Villages of Orange Blossom Gardens.

Lastly, I would like to acknowledge my family and friends who have always been there to provide the needed support and encouragement: my parents for their love, understanding, and willingness to help in any way; Sarah and Tim for their cooperation and for reminding me how to laugh; and finally, to my husband, Stephen, for his loving support and "life-saving" assistance throughout this entire project. I could not have done this without you. I would also like to extend my sincere appreciation to Ellen and Rick Bush whose editing and computer expertise made this manuscript possible.

TABLE OF CONTENTS

LIST OF TABLES

Abstract of Thesis Presented to the Graduate School
of the University of Florida in Partial Fulfillment
of the Requirements for the Degree of
Master of Science in Nursing

RELATION BETWEEN CIGARETTE SMOKING, BODY FAT DISTRIBUTION AND DENSITY OF LIPOPROTEIN CHOLESTEROL IN WOMEN

By

Linda R. Beson

August 1992

Chairperson: Sandra Seymour
Major Department: Nursing

Coronary heart disease is the number one killer of American women; however, most scientific research regarding risk factors for disease has focused on men. The purpose of this study was to describe the relation between cigarette smoking, distribution of body fat, and density of lipoprotein cholesterol in women. Variables selected for study were total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, cigarette smoking, and the waist to hip circumference ratio.

The sample consisted of 75 adult women volunteers, ages 22 to 74 years. Data were collected at three sites over a four week period. Statistically significant correlations were found between an increased waist to hip circumference ratio and decreased HDL-cholesterol, and increased

triglycerides. No significant correlation was found between the waist to hip ratio and total cholesterol or LDL-cholesterol. Finally, no significant correlation was found between cigarette smoking and an increased waist to hip ratio or decreased HDL-cholesterol.

CHAPTER I
INTRODUCTION

Cardiovascular disease is the leading cause of death among men and women in the United States, accounting for more deaths each year than all forms of cancer and other diseases combined (American Heart Association, 1988). Coronary heart disease (CHD) results in 550,000 of these cardiovascular deaths each year, of which over 250,000 are women (Eaker, Packard, Wenger, Clarkson, & Tyroler, 1987). Approximately 100,000 of the deaths due to CHD occur prematurely, or before the average life expectancy of 78 years for women (Thom, 1987).

The total cardiovascular disease mortality rate has declined among both men and women since the 1940s. Trends in CHD mortality, however, demonstrate some age and sex differentials (Thom, 1987).

The decline in CHD mortality from 1962 to 1978 was marked in all age, race, and sex groups, but began earlier among women than among men. Declines since 1979 have been steeper among men than among women, lowering the male-female ratio of CHD death rates for the first time (Thom, 1987). This continuous decline in CHD mortality rate is not clearly understood, but supports the theory that the development of coronary artery disease can be delayed or prevented through

appropriate interventions such as life-style changes and methods of treatment (Thom, 1987).

Because men experience a two- to threefold greater risk of CHD compared with women and develop it at a younger age, the focus of most research has been on middle-aged men (Eaker et al., 1987). Women have been excluded from most studies or represented in such small numbers that an accurate assessment of gender-related differences in CHD etiology, clinical manifestations, and expected therapeutic outcomes have not been possible. Nevertheless, most diagnostic and intervention decisions for women have been based on these data obtained from research with men (Leaf, 1988; Wenger & Roberts, 1987). The assumption that the results are equally applicable to women is questionable considering the physiological differences that have been identified in male and female responses.

Women seem to be protected from developing CHD during their reproductive years and typically demonstrate a lag in coronary incidence of about 10 years behind that of men (Wenger, 1985). It is not clear why this occurs but could be related to a protective effect of estrogens and their role in promoting higher levels of cardioprotective high density lipoprotein (HDL) cholesterol (Clarkson, 1987; Leaf, 1988). When comparing the amount of aortic surface involvement by atherosclerotic lesions at autopsy, Strong's findings revealed that men have approximately 50% more atherosclerosis than women (cited in Leaf, 1988).

Another example of a gender-related, physiological difference is in the male and female cardiovascular response to exercise. Since the male pattern of response to exercise has been studied more extensively, it is generally accepted as "normal". Since men normally exhibit at least a 5% increase in ejection fraction with exercise, failure to increase the ejection fraction by 5% indicates abnormal cardiac function and/or abnormal myocardial perfusion. The results of a study of age-matched volunteers revealed that women did not exhibit this response, but instead increased their left ventricular end-diastolic volume (Higginbotham, Morris, Coleman, & Cobb, 1984). These findings indicate that normal, middle-aged men and women achieve increases in stroke volume during upright exercise by different mechanisms. Diagnostic testing will not be as accurate in women if a normal response is defined by reference values that do not apply to them (Douglas, 1986).

The initial presentation of CAD is also different in women, with angina being the likely presentation rather than myocardial infarction or sudden death (Wenger, 1985). Fewer than 50% of women with angina, however, have significant coronary artery disease on angiography (Chaitman et al., 1981; Proudfit, Shirey, & Sones, 1966). The results of several studies have demonstrated that women generally have a much worse prognosis following a myocardial infarction as compared to men (Greenland, Reicher-Reiss,

Goldbourt, & Behar, 1991; Kannel & McGee, 1979; Puletti, Sunseri, Curione, Erba, & Borgia, 1984). Wong's investigation adjusted for age and standard coronary risk factors and a substantial coronary survival advantage was shown in women (Wong, Cupples, Ostfeld, Levy, & Kannel, 1989).

The Coronary Artery Surgery Study (CASS) results revealed that the operative mortality for women was 2.7 times greater than that for men, even though women generally demonstrated less severe coronary disease and better ventricular function (Mock et al., 1982).

Risk factors that predict the occurrence of CHD have been utilized to establish the framework for preventative interventions. Most of the research that identified risk factors and subsequently evaluated the effectiveness of interventions designed to modify those risk factors was done with men. Preventative health measures that have been successful in lowering the incidence of CHD in one sex do not necessarily afford the same benefit to the other. Several risk factors have been identified that are unique to women, including menopause, post-menopausal hormones, and the use of oral contraceptives (Corrao, Becker, Ockene, & Hamilton, 1990). It is also uncertain whether the weight of risk factors and their interrelations are the same among women as among men.

Despite the recent decline in the mortality rate, CHD still accounts for 28% of all deaths of women in the United

States (Eaker et al., 1987). As the age of the general population increases, there will tend to be a greater number of women with CHD. In 1980, women generated approximately 58% of all expenditures for heart disease, estimated at 7.6 billion dollars (Eaker et al., 1987). Identification of gender-related differences in CHD risk factors will establish the framework for more appropriate preventative interventions in women. These specific risk factor modifications could result in reduced overall morbidity and mortality and lower health care expenditures.

Purpose of the Study

The purpose of this research was to describe the relation between cigarette smoking, distribution of body fat, and density of lipoprotein cholesterol in women.

Hypotheses

(1) Cigarette smoking will correlate with an increased waist to hip circumference ratio (apple shape) and decreased HDL-cholesterol.

(2) An increased waist to hip circumference ratio (apple shape) will correlate with decreased HDL-cholesterol, increased triglycerides, and increased total and LDL-cholesterol.

Definition of Terms

For the purpose of this research, the following definitions are used:

Risk factors are genetic and environmental variables statistically related to CHD (Hjermann, 1985).

Cardiovascular disease is the encompassing term that includes a multitude of disease processes involving the heart and blood vessels. This term includes heart disease, hypertension, stroke, and kidney disease (Thom, 1987).

Coronary heart disease is also known as ischemic heart disease and is defined as a disorder of the coronary arteries that disrupts blood flow to the myocardium. This term includes angina, myocardial infarction, cardiac ischemia, and sudden death (Thom, 1987).

Obesity will be defined in terms of the body mass index (BMI) which is calculated by dividing the body weight in kilograms by the height in meters squared. A BMI exceeding 30 defines obesity. A BMI of 25-30 will be defined as overweight (Bray & Gray, 1988).

Waist to hip circumference ratio is a means of estimating the amount of abdominal fat content. A higher ratio of waist to hip circumference (apple shape) indicates central fat distribution or the masculine pattern. A lower ratio (pear shape) indicates the female pattern of fat distribution (Hartz et al., 1990)

Coronary risk profile is a method developed by the American Heart Association to compile identified risk factors in a particular individual and estimate the probability of a coronary event occurring within five or ten years (Anderson, Wilson, Odell, & Kannel, 1991).

Assumptions

Assumptions basic to this research are

1. The probability of developing coronary heart disease can be predicted by risk factors (Dawber & Meadors, 1951; Leaf, 1988).

2. The major risk factors of age, blood pressure, cigarette smoking, and plasma lipoprotein concentration that have shown a predictive relationship to CHD in men are also predictive of CHD in women (Leaf, 1988; Wenger, 1985).

Limitations

The following limitations apply to this investigation:

1. Results of only one blood sample will be used for comparison to the other research variables. It has been demonstrated that serum cholesterol, triglyceride, and lipoprotein levels can fluctuate considerably from day to day in a given individual and more than one measurement should be obtained in order to accurately assess the person's serum lipid status (Knoke & Hawkins, 1985; Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults [Report of the Expert Panel], 1988).

2. Serum lipoprotein cholesterol levels were performed in two different laboratories. The method of analysis used was noted and standardized.

CHAPTER II
REVIEW OF THE LITERATURE

This chapter contains a review of the literature related to risk factors for coronary heart disease, focusing on how the results of previous research may and may not be related to women. Emphasis is given to research related to cholesterol, serum lipoproteins, body fat distribution and cigarette smoking.

Risk Factors

Risk factors describe the association between coronary heart disease (CHD) and selected genetic, acquired, and environmental factors. A cause-and-effect relationship is not necessarily implied by this association, but several characteristics strengthen this correlation. Hjermann (1985) states that:

> The statistical associations are considered more likely to be causal if the risk factor precedes the disease, if the association is strong and dose-related, consistent, predictive of disease in other population samples, independent of other risk factors, pathogenetically plausible, and supported by experimental research and clinical investigations. (p. 1)

Investigation into the cause of coronary heart disease began in 1948 with the Framingham Heart Study (Dawber & Meadors, 1951). This prospective study, which is still ongoing, has provided the majority of data concerning gender

differences in CHD incidence, morbidity, and mortality (Becker, 1990). Age, cigarette smoking, hypertension, plasma lipoprotein concentrations, diabetes, obesity, physical inactivity, stress, "Type A" personality characteristics, and family history of heart disease have all been identified as "risk factors" for the development of CHD in men and women (Corrao et al., 1990). The role and/or interactions of some of these risk factors such as obesity, use of estrogen hormones, physical activity, and personality and stress in the development of the disease may be different and unique for women (Leaf, 1988).

The weight of several risk factors has been shown to vary between men and women. The Framingham Heart Study revealed that for men, risk factors of coronary disease were also predictive of sudden death, supporting the theory that sudden death is related to atherosclerosis (Douglas, 1986; Schatzkin et al., 1984). In women, however, hematocrit and vital capacity were found to be significant predictors of sudden death while systolic blood pressure, smoking history, and obesity were unrelated (Douglas, 1986; Schatzkin et al., 1984). The results of several studies demonstrated that diabetes is a stronger risk factor for CHD mortality among women than among men (Barret-Connor & Wingard, 1983; Heyden, Heiss, & Bartel, 1980; Kannel & McGee, 1979). Another finding was the variability in risk factor significance in

different age groups. Characteristics that are not consistent across age groups are serum cholesterol levels, use of blood pressure medications, postmenopausal hormone use, and triglyceride levels (Eaker & Castelli, 1987).

The risk factors have been used to establish the framework for preventative interventions. Considering the many gender-related differences that have been identified in the development and response to CHD and its treatment, and the fact that most of the research related to disease prevention has been done on male subjects, the current recommendations for risk reduction may be limiting our effectiveness in reducing overall morbidity and mortality (Douglas, 1986; Leaf, 1988).

Despite the gender-related differences that have appeared in the research regarding the influence of risk factors, strong evidence supports the idea that major risk factors (age, cigarette smoking, hypertension, and elevated cholesterol) are at least as predictive for women as they are for men. Approximately 60% of new CHD events among women in the Framingham Heart Study occur in the top quintile of risk in contrast to fewer than 50% of new CHD events that occur in the top quintile of risk among men (Epstein, 1987).

If the same major risk factors affect men and women, it seems logical to assume that the intervention strategies that have been successful in reducing the incidence of CHD in men should also be effective in women. A strong supporting

factor of this assumption is that the cardiovascular death rate in women has declined by 43% between 1963 and 1983 with most of the decline occurring after 1972 (Thom, 1987). The reasons for this decline are not clear, but could reflect the life-style changes such as reduction in saturated fat intake and cigarette smoking that have occurred in our population during this period (Goldman & Cook, 1984). More evidence is needed to substantiate the hypothesis that the modification of the risk factors accounts for the decline in mortality rate.

Risk factor analysis is a process used to predict the development of coronary heart disease in individuals free of disease (Kannel, McGee, & Gordon, 1976). The first handbook with CHD risk tables was published in 1973 and was based on calculations made from the Framingham data base (American Heart Association's Coronary Risk Handbook--Estimating the risk of coronary heart disease in daily practice: cited in Anderson, Wilson, Odell, & Kannel, 1991). The risk factors that were originally considered were: age, gender, systolic blood pressure, serum cholesterol, cigarette smoking, glucose intolerance, and left ventricular hypertrophy (Anderson et al., 1991). The findings from Framingham and other epidemiological studies have supported the theory that CHD risk can be predicted in large population samples before symptoms are evident (Kannel et al., 1976; Brand, Rosenmon, Sholtz, & Friedman, 1976; Leaverton et al., 1987).

An update of the earlier risk handbook determines an individual's probability of experiencing a coronary event within five and ten years of the assessment (Anderson et al., 1991). This coronary risk profile is based on the larger and more recent data base from the Framingham Heart Study which adds HDL-cholesterol to the risk profile (Anderson et al., 1991).

Generally, the more risk factors present and the more pronounced the abnormalities, the higher the risk score. Several limitations to the coronary risk profile have been identified: (1) it can only be used on risk factors measured, (2) predictions may not be appropriate for individuals with extremely elevated risk factors, (3) predictions may not be applicable to populations with a very low CHD incidence rate, and (4) it may not necessarily apply to persons who already have CHD (Anderson et al., 1991).

Body Fat Distribution

The relation of obesity to coronary heart disease remains controversial. Much of the research done in this area has been unable to consistently demonstrate an independent effect between obesity and cardiovascular disease (Larsson, Bjorntorp, & Tibblin, 1981). Interestingly, the association between obesity and cardiovascular risk factors remained in these studies, even though they were unable to demonstrate an association between obesity and cardiovascular

disease (Larsson et al., 1981). The only studies that showed a relation between obesity and cardiovascular disease were long-term investigations of 10-26 years (Lapidus et al., 1984). A report from the Framingham study identified obesity as a risk factor for cardiovascular disease, independent of age, systolic blood pressure, serum cholesterol concentration, cigarette smoking, and glucose intolerance. The independent effect was even more pronounced in women, particularly in those less than 50 years of age. For each pound above ideal weight gained over the first 26 years of the Framingham Study, the death rate increased by 2% (Hubert, Feinleib, McNamara, & Castelli, 1983).

One possible explanation for the discrepancies described in these studies is that only part of the obesity syndrome is associated with risk of cardiovascular disease. Subsequent research has consistently suppported the theory that abdominal obesity is a subgroup of human obesity in which the risk of cardiovascular disease is concentrated (Hartz et al., 1990; Lapidus et al., 1984; Larsson et al., 1984). A simple index used to identify upper body and abdominal obesity is a waist to hip circumference ratio (Freedman et al., 1990). Abdominal obesity (android or apple shape) is indicated by a high ratio of waist to hip circumference. A ratio of 0.85 or higher indicates high risk (Leaf, 1990).

Central adiposity is also associated with certain metabolic complications such as diabetes, hypertension, and altered plasma lipids that are known to increase the risk

for cardiovascular disease (Despres, Moorjani, Lupien, Tremblay, & Bouchard, 1990). It is possible that the independent effect of body fat distribution on cardiovascular disease results from these metabolic disturbances (Despres et al., 1990).

Cholesterol and Serum Lipoproteins

The effects of cholesterol on coronary heart disease have been examined for over 40 years and there is very little doubt that total cholesterol is a major risk factor (Kannel, Castelli, Gordon, & McNamara, 1971; Pooling Project Research Group, 1978; Stamler, Wentworth & Neaton, 1986). Coronary risk rises progressively with an increase in the total cholesterol level, particularly when the level is greater than 200 milligrams per deciliter (mg/dL) (Report of the Expert Panel, 1988). Evidence indicates that lowering total cholesterol levels can decrease the incidence of CHD, however, specific studies in women have not been done (Coronary Drug Project, 1975; Manninen et al., 1988; The Lipid Research Clinics Coronary Primary Prevention Trial Results II [Lipid Research Clinics Program II], 1984). For every 1% decrease in total cholesterol, CHD risk has been shown to decrease by 2% (Lipid Research Clinics Program II, 1984). According to Grundy (1986), the incidence of CHD could be decreased by 30-50% if most persons could maintain an ideal total cholesterol level of 130-190 mg/dL.

This link between serum cholesterol and CHD is related to the role of cholesterol in the development of

atherosclerosis. Cholesterol is an important and essential structural component of cell membranes, provides a source of free fatty acids, and is a precursor of the corticosteroid hormones estrogen, progesterone, and testosterone. Eighty percent of the body's cholesterol is used to make bile acid (Guyton, 1987). Cholesterol has also been implicated in the arterial plaque formation that results in atherosclerosis.

The prevailing "response-to-injury" theory, states that plaque formation begins with damage to the endothelial layer of the arterial wall and progresses as low-density lipoprotein (LDL) particles from the elevated serum cholesterol are incorporated into the injured area. The precise mechanism involved in this process has not been determined. The cholesterol in the lesion eventually calcifies into a hard plaque or atheroma that protrudes into the arterial bloodstream and can eventually obstruct blood flow (Memmer, 1989). The probability of developing symptomatic CHD dramatically increases when approximately 60% of the coronary artery lumen is obstructed with plaque (Grundy, 1986; Strong, Solberg, & Restrepo, 1968). The development of atheromas can be stopped and the size of the plaque actually decreased when serum cholesterol is substantially reduced (Blankenhorn et al., 1987; Memmer, 1989).

Humans obtain cholesterol both exogenously, from animal products consumed in the diet, and endogenously, from synthesis in the liver and other tissues (Gordon &

Rifkind, 1989). The relative importance of exogenous or in vivo sources of cholesterol has not been established. Education programs promoted by the American Heart Association (AHA) and the National Heart, Lung and Blood Institute (NHLBI) have focused on diet modifications to reduce fat and cholesterol intake in an effort to lower serum cholesterol levels and reduce risk for developing CHD (AHA, 1989; NHLBI, 1989).

Another interesting theory that attempts to explain the link between cholesterol and CHD claims that cholesterol does not become atherogenic until it is oxidized and converted to one or more of a number of autoxidation products (Addis & Warner, 1991). A key step in atherosclerosis is the attachment of the LDL particle to the vessel wall with resultant lipid accumulation. This "lipid oxidation theory" postulates that LDL particles must contain lipid oxidation products before they can be recognized by the monocytes in the vessel wall. Cholesterol oxidation products are found in many common processed foods such as powdered eggs, freeze-dried meats, and dehydrated cheese and butter powders. French-fried foods are a major source of dietary oxidation products. Heating oil forms fatty acid degradation products and cholesterol oxides regardless of whether a vegetable shortening or animal fat is used (Addis & Warner, 1991).

Proponents of the "lipid oxidation theory" claim that dietary (pure) cholesterol is not angiotoxic nor hypercholesterolemic and, therefore, cannot initiate or

promote CHD. They theorize that it is the lipid oxidation product consumption patterns rather than cholesterol intake that may partially explain why some individuals with high serum cholesterol do not develop CHD and why some individuals with low serum cholesterol have CHD. In general, however, lowering dietary lipid content will also result in lowering an individual's exposure to lipid oxidation products (Addis & Warner, 1991).

Cholesterol and triglycerides are the major plasma lipids. All lipids in plasma combine with protein and circulate as lipoproteins (Schaefer & Levy, 1985). Plasma lipoproteins are spherical particles with a surface composed largely of phospholipid, free cholesterol, and apoprotein and a core consisting mostly of triglycerides and cholesterol ester (Jackson, Morrisett, & Gotto, 1976). Plasma lipoproteins are divided into five types, depending on their density, composition, and electrophoretic mobility. Density is determined by their relative content of protein and lipid (Talbert, 1989). The many ways in which cholesterol is transported by the body's complex system of lipoproteins is still not completely understood.

Chylomicrons are large triglyceride-rich particles that have the lowest density and are secreted by the intestine after meals. Chylomicrons deliver triglycerides to adipose tissue for storage and to muscle where the triglycerides are used for energy. These particles are normally not found in the plasma after a fast of 12-14 hours (Talbert, 1989).

Very-low-density lipoprotein (VLDL) is secreted by the liver and is the major triglyceride carrier in plasma (Gordon & Rifkind, 1989). Intermediate-density lipoprotein (IDL) is a transient product of VLDL catabolism and a precursor of LDL (Gordon & Rifkind, 1989). Low-density lipoprotein (LDL) is the main cholesterol-carrying particle in the plasma and is the lipoprotein most strongly correlated with atherosclerosis. Low-density lipoprotein primarily transports cholesterol to the body cells (Cotran, Kumar, & Robbins, 1989).

Not all circulating lipoproteins are potentially atherogenic. High-density lipoprotein particles, commonly referred to as "the good cholesterol", are usually low in cholesterol and rich in phospholipids (Gordon & Rifkind, 1989). They are hypothesized to be involved in the "reverse transport" of cholesterol from peripheral tissues to the liver where it is excreted rather than re-utilized in further synthesis of LDL (Cotran et al., 1989). This anti-atherogenic role of HDL could therefore be related to the direction in which it transports the cholesterol rather than to any unique property of its cholesterol, but this has yet to be established (Gordon & Rifkind, 1989).

Low Density Lipoprotein (LDL) Cholesterol

Numerous epidemiologic studies and clinical trials have specifically identified elevated LDL-cholesterol as a risk factor for the development of CHD (Grundy, 1986; Kannel,

Castelli, & Gordon, 1979; Pooling Project Research Group, 1978; The Lipid Research Clinics Coronary Primary Prevention Trial Results I [Lipid Research Clinics Program I], 1984). In the average American, 70% of the cholesterol in the plasma is found in the LDL, so the total cholesterol level is closely correlated with the concentration of LDL-cholesterol (Cotran et al., 1989; Report of the Expert Panel, 1988). Premature CHD has developed in individuals, including children, who have an elevated LDL-cholesterol level without any other risk factors (Schaefer & Levy, 1985).

The rise in serum cholesterol noted with age is not completely understood, but has been attributed to increased production of LDL and decreased clearance of LDL via the LDL receptors on liver cells and by extrahepatic tissues (Grundy, Vega, & Bilheimer, 1985; Grundy, 1986). Substantial evidence also indicates that lowering LDL-cholesterol levels will reduce the incidence of CHD, but again, specific studies on women have not been done (Coronary Drug Project, 1975; Lipid Research Clinics Program-I, 1984; Lipid Research Clinics Program-II, 1984; Manninen et al., 1988). Finding individuals with elevated LDL-cholesterol levels is the ultimate objective of screening according to The National Cholesterol Education Program. The level of LDL-cholesterol is then used as the key index for clinical decision making about cholesterol-lowering therapy (Report of the Expert Panel, 1988).

High Density Lipoprotein (HDL) Cholesterol

Epidemiologic data from Framingham and other studies indicate that levels of HDL-cholesterol have a strong inverse relationship to CHD risk (Gordon, Castelli, Hjortland, Kannel, & Dawber, 1977; Miller & Miller, 1975; Miller, Thelle, Forde, & Mjos, 1977). The Framingham Study extended earlier findings and demonstrated that HDL-cholesterol is a very important CHD risk factor at any given level of LDL-cholesterol (Castelli et al., 1986). These findings have also been supported in numerous lipid intervention studies and coronary angiographic studies (Arntzenius et al., 1985; Jacobs, Mebane, Bangdiwala, Criqui, & Tyroler 1990; Lipid Research Clinics Program-I, 1984; Lipid Research CLinics Program-II, 1984; Manninen et al., 1988; Pearson, Bulklye, Achuff, Kwiterovich, & Gordis, 1979). It has definitely been established that a low HDL level is an important coronary risk predictor in men and women, but it is uncertain whether it is a causative or a coincidental factor (Pearson et al., 1979; Wilson, Abbott & Castelli, 1988).

The results of four large prospective epidemiologic studies demonstrated that for every 1-mg/dL rise in HDL-cholesterol, CHD risk fell about 2% in men and 3% in women and cardiovascular mortality fell by 4% in men and 5% in women (Gordon et al., 1989). Considering the association between lower HDL levels and higher rates of CHD, it seems logical to propose that raising low levels of HDL-cholesterol

will lower the incidence of CHD. The Helsinke Heart Study revealed a significant decrease in the incidence of CHD when HDL-cholesterol was raised and LDL-cholesterol was lowered using gemfibrozil (Manninen et al., 1988). These results suggest that increasing HDL levels may decrease the risk of CHD; however, no experimental evidence exists that specifically demonstrates this relationship (Manninen et al., 1988). No clinical trial has actually tested the results of raising low HDL levels or targeted individuals with low levels of HDL-cholesterol for intervention (Gordon & Rifkind, 1989).

Cross-cultural comparisons of HDL-cholesterol levels and incidence of CHD in nonindustrialized and industrialized countries have revealed conflicting results. Low rates of CHD are commonly found in nonindustrialized populations with low levels of HDL and total cholesterol when the consumption of fat is low (Knuiman, West, Katan, & Hautvast, 1987). Low rates of CHD are also found in vegetarians and others who consume low fat diets with high ratios of polyunsaturated to saturated fat, even though they tend to have relatively low levels of both HDL and LDL-cholesterol (Sacks et al., 1985). Gordon and Rifkind (1989), speculate that low levels of HDL-cholesterol may be a risk factor mainly in populations that consume a high-fat diet.

Another complicating aspect to the association of low levels of HDL-cholesterol with high rates of CHD is the fact that levels of HDL are also inversely correlated with plasma

triglyceride levels (Heiss, Johnson, Reiland, Davis, & Tyroler, 1980). Although not well understood, cholesterol molecules in the core of HDL particles are transferred to VLDL particles in exchange for triglyceride molecules (Austin, 1989). In addition, numerous CHD risk factors associated with low HDL-cholesterol such as sedentary habits, obesity, diabetes, and smoking, are also associated with higher levels of triglycerides (Heiss et al., 1980).

Triglycerides

A high percentage of individuals with CHD have elevated triglycerides (Grundy & Vega, 1992). The level of plasma triglyceride has been associated with an increased risk for CHD in many case-control, cross-sectional, and prospective studies, however, inconsistent results have led to doubt regarding the significance of this association (Austin, 1991). In addition, triglyceride is not found in large amounts in atherosclerotic plaques as cholesterol is, leading to the hypothesis that triglyceride is a marker for higher risk of CHD or possibly plays an indirect role in causing CHD (Grundy & Vega, 1992).

The majority of dietary fat consumed in the United States is triglycerides composed of long-chain fatty acids. After ingestion, triglycerides are broken down into free fatty acids and monoglycerides and absorbed into the intestinal wall (Castelli, 1986). The small amounts of short or middle-chain fatty acids found in the American diet are bound to albumin and carried directly to the liver. The

long-chain fatty acids are absorbed into the intestinal cell as the monoglyceride, re-formed into triglyceride, and combined with specific apolipoproteins to be transported in the blood stream as chylomicrons (Castelli, 1986).

Exogenous triglyceride is carried in chylomicron particles and endogenous triglyceride is carried in VLDL particles (Austin, 1989). Chylomicrons are broken down into free fatty acids on the cell membranes throughout the body where they are absorbed to provide energy (Austin, 1989). This process leaves the chylomicron remnant, a cholesterol-rich particle that returns to the liver. Endogenous triglyceride is synthesized in the cells of the liver from these sources of free fatty acids and is carried in VLDL particles. In addition, the liver also converts excess calories from carbohydrate, protein, and alcohol to fatty acids and then to triglycerides to produce additional VLDL particles (Castelli, 1986). After an individual fasts for 12 hours, chylomicrons are normally not present, and triglyceride is primarily carried in the VLDL particles (Austin, 1989).

Almost all studies have found a univariate association between triglyceride and CHD (Goldstein et al., 1973; Holmes et al., 1981; Patterson & Slack, 1972). However, the results of multivariate analyses with other lipid and lipoprotein variables are highly variable and triglyceride often loses its independent association and is no longer considered a

significant predictor of CHD (Freedman, Gruchow, Anderson, Rimm, & Barboriak, 1988; Gordon, Castelli, Hjortland et al., 1977; Hulley, Rosenman, Bawol, & Brand, 1980). No intervention study has been done to specifically evaluate triglyceride-lowering effects on prevention of CHD (Austin, 1991).

According to Austin (1989), the apparent discrepency between univariate and multivariate statistical results is a combination of 1) the large variability of the triglyceride measurements, both within and between individuals, and 2) the strong inverse correlation between triglyceride and HDL-cholesterol. These two factors can result in an underestimate of the triglyceride association to CHD when using multivariate analysis. Manninen et al., (1992) states that:

> Due to multicollinearity, it is not appropriate to adjust for HDL-cholesterol when studying the association between serum triglycerides and CHD. An independent association between triglycerides and CHD may have no biological meaning, as the metabolisms of triglyceride-rich VLDL, and HDL and LDL are closely interrelated. (p. 37)

Grundy and Vega (1992) describe two different views to explain the relationship of triglycerides to CHD: 1) VLDL may be directly atherogenic and 2) metabolic consequences of hypertriglyceridemia such as elevated postprandial lipoproteins, large VLDL particles, small, dense LDL particles, low levels of HDL-cholesterol, and possibly a procoagulant state account for the association. These relationships are still not completely understood.

Although most research has been done with men, several studies have specifically investigated triglyceride as a risk factor for CHD in women. Results are variable, however, triglycerides were reported to be at least a univariate risk factor in most studies (Austin, 1991). The early reports from the Framingham Study indicate that triglycerides are a strong predictor of CHD in women over age 50 in the univariate and multivariate analyses (Castelli, 1986). The 14-year follow-up report from the Framingham study demonstrated similar results, however, the relation was no longer significant after adjusting for HDL-cholesterol (Wilson, Anderson, & Castelli, 1991).

Elevated triglycerides were more strongly associated with CHD in women than serum cholesterol levels were in several other studies. The results of The Lipid Research Clinics Follow-up study indicated that elevated triglycerides were an even greater risk for women than men (Criqui, 1991). Johansson et al. (1988) studied younger women less than 55 years of age with an acute myocardial infarction (MI) and found high serum triglycerides were independently and significantly associated with MI, but serum cholesterol levels were not. Another study reported high levels of triglycerides predicted the severity of atherosclerosis measured by arteriography better than high levels of serum cholesterol (Reardon, Nestel, Craig, & Harper, 1985). One study, however, found no significant association between triglycerides and CHD mortality in women (Simons, 1986).

Gender-related Differences in Lipoprotein Concentrations

Men experience a two-to-threefold greater risk of CHD compared with women and develop it at a younger age. This gender-related difference in CHD susceptibility is not completely understood, but is commonly attributed to gender-related differences in serum lipoprotein concentrations. Women in the United States between the ages of 20 and 50 years theoretically have a more favorable lipid profile than men with lower levels of plasma LDL-cholesterol and VLDL-cholesterol and higher levels of HDL-cholesterol (Godsland, Wynn, Crook, & Miller, 1987).

The following findings have promoted the widely accepted hypothesis that gender-related differences in lipoprotein concentrations are due to hormonal differences between men and women: 1) changes in serum estrogen and androgen concentrations are associated with changes in lipoprotein levels 2) women appear to have higher LDL and VLDL levels after the age of menopause when estrogen levels are decreased; this coincides with an increased incidence of CHD in women 3) the gender-related difference appears to be present in all countries in which CHD is a significant cause of death (Godsland et al., 1987).

Research regarding the relation between gonadal steroids and serum lipoprotein levels has been conducted for over 30 years and the generally accepted hypothesis is that androgens

decrease HDL-cholesterol and increase LDL-cholesterol, and estrogens increase HDL-cholesterol and decrease LDL-cholesterol (Godsland et al., 1987).

Some of the data, however, reveal information that is inconsistent with this hypothesis. Very little difference is found in serum lipoprotein levels between men and women in societies where CHD is rare, indicating that basic physiologic differences between men and women cannot completely explain the differences in lipoprotein levels (Godsland et al., 1987; Hosaki, Kishimoto, Yamauchi, & Shiina, 1985; Kesteloot et al., 1985).

Most of the evidence relating gender differences in lipoprotein risk factors to the effects of circulating gonadal hormones comes from studies of changes in gonadal status or of the effects of synthetic hormones rather than from normal men and women (Godsland et al., 1987). Synthetic hormones expose the liver to hormonal levels that are much higher than the normal physiologic levels and are structurally different from natural hormones (Gordon & Rifkind, 1989). The lipoprotein changes noted with their use may be due to the pharmacologic actions of these preparations and may not accurately reflect the relation of natural hormones to lipoprotein changes that occur in the body (Godsland et al., 1987).

Another interesting factor to consider is that boys and girls have similar levels of HDL-cholesterol until puberty when increasing levels of testosterone correlate with

decreasing levels of HDL-cholesterol in boys. No significant change is noted in the level of HDL-cholesterol in girls when estrogen levels rise during menarche (Gordon & Rifkind, 1989). In addition, the slowing of the rate of increase in levels of LDL and VLDL that occur in men after the age of 50 correspond with decreasing serum testosterone levels, suggesting that testosterone, rather than estrogen, may be the determining factor (Godsland et al., 1987).

The belief that estrogen has a protective effect for women in the development of CHD has been based on the decreased male-female ratio of CHD death rates that occurs around the age of 50 and the changes in lipoprotein concentrations caused by the administration of estrogens, however, there is no definitive evidence for this. The changes noted in lipoprotein levels at the time of menopause may simply reflect age-related changes rather than hormone-related changes.

In women, the upward trend in cholesterol, LDL, VLDL and triglyceride levels with age is continuous before, throughout, and after menopause. High density lipoprotein (HDL)-cholesterol shows little change with age and remains consistently higher in women (Godsland et al., 1987). In men, VLDL and triglyceride levels peak around age 45 to 50 and then decline. Also, the rate of increase in LDL levels begins to decrease at 50 years of age and women begin to overtake levels in men for the first time (Godsland et al., 1987). These changes in cholesterol and lipoprotein levels

diminish the gender-related differences in lipoprotein risk status for CHD at the age most women experience natural menopause. It is possible, therefore, that the decreased male-female ratio of CHD death rates at this time is due to the decline in death rates in men rather than to an acceleration in CHD incidence in women due to menopause (Godsland et al., 1987).

National mortality data have not supported the hypothesis that menopause causes an increase in the rate of death from CHD (Tracy, 1966). When the death rate was plotted on a semilogarithmic scale against age, a constant rate of increase in the rate of CHD mortality was seen throughout youth to old age in women. No increase was demonstrated during the age range when women are menopausal (Tracy, 1966). Data from the United Kingdom actually demonstrated a decline in the rate of increase in CHD mortality rate in women after the menopause (Heller & Jacobs, 1978).

There is very little doubt that serum cholesterol is related to atherosclerosis and the incidence of CHD in both men and women. It is evident from the number of studies conducted and the conflicting results reported that complex interrelations exist between cholesterol and triglyceride metabolism and lipoprotein transport. A well accepted theory relates the higher incidence of CHD in men to the differences in serum lipoprotein risk factors between men and women.

Sex hormones clearly affect lipoprotein metabolism, however, it remains uncertain exactly how much, if any, of these effects account for the gender-related differences in CHD incidence.

Cigarette Smoking

Cigarette smoking is a well documented risk factor for the development of acute myocardial infarction (MI), and sudden death in men and women (Doyle, Dawber, Kannel, Kinch, & Kahn, 1964; Hammond & Horn, 1958; The Pooling Project, 1978; Rosenberg et al., 1985). Smoking has not, however, been consistently associated with the incidence of uncomplicated angina pectoris (Kannel, McGee, & Castelli, 1984; Wilhelmsen et al., 1986). It is still unclear exactly how cigarette smoking acts biologically to account for 30% to 40% of the 565,000 deaths from CHD in the United States, but a combination of several mechanisms is probably involved (Criqui et al., 1980; FitzGerald, Oates, & Nowak, 1988; Kannel, 1981). Both nicotine and carbon monoxide are the likely causative factors of most of the acute effects (Robertson, Tseng, & Appalsamy, 1988).

Cigarette smoking results in adverse changes in lipid metabolism that could promote CHD and atherosclerosis. Nicotine has been shown to stimulate the sympathoadrenal system which results in lipolysis and free fatty acid mobilization from adipose tissue (Mjos, 1988). Elevated levels of free fatty acids increase myocardial oxygen consumption and, in turn, oxygen demand (Mjos, 1988).

Increased levels of LDL-cholesterol commonly found in smokers could also result from this adrenergic activity (Memmer, 1989). Smokers are also noted to have lower levels of HDl-cholesterol than nonsmokers and heavier smokers (greater than 20 cigarettes per day), have lower HDL levels than lighter smokers (Criqui et al., 1980; Garrison et al., 1978). Considering the many biologic, environmental, and behavioral characteristics that have been shown to influence HDL-cholesterol, Criqui et al. (1980) adjusted for age, hormone use, alcohol intake, physical activity, and body mass and found cigarette smoking was still independently and significantly related to decreased HDL-cholesterol in men and women. This does not appear to be a permanent change, however, since the mean HDL-cholesterol levels of ex-smokers were similar to those of nonsmokers (Criqui et al., 1980).

Evidence linking cigarette smoking with coronary atherosclerosis is inconclusive. Smoking has been shown to damage endothelial cells and autopsy studies of young male smokers have demonstrated a positive association between cigarette smoking and the extent of coronary atherosclerosis (Auerbach, Hammond, & Garfinkel, 1965; Fitzgerald et al., 1988). It is suspected that carbon monoxide and other chemical derivatives of smoke may enlarge atheromas by enhancing damage to the arterial lining and increasing the permeability of arterial walls to lipoproteins (Castelli, Dawber, Feinleib et al., 1981; Memmer, 1989). Overall, heavy smokers seem to have slightly to moderately more extensive

advanced coronary atherosclerosis, however, the difference does not seem significant enough to explain the twofold or greater risk of developing CHD commonly found in smokers (McGill, 1988). The excess risk of cardiovascular events in smokers decreases by 50% within the first year after stopping smoking and ex-smokers experience no excess risk after five years (McGill, 1988). These data along with the strong association demonstrated between MI and smoking and the weaker association with angina pectoris suggest that other mechanisms, in addition to atherosclerosis, play an important role in the development of CHD in smokers (Kannel et al., 1984).

According to one prominent theory, smoking affects the risk of CHD predominantly by increasing the risk of intracoronary thrombosis (McGill, 1988; Wilhelmsen, 1988). Smokers have elevated plasma fibrinogen levels and an increase in platelet aggregability (O'Connor, Cederholm-Williams, Copper, & Cotter, 1984; Renaud, Blache, Dumont, Thevenon, & Wissendanger, 1984). A direct association between plasma fibrinogen concentration and the incidence of ischemic heart disease has been demonstrated in prospective studies. This association was even more pronounced than for serum cholesterol (Meade et al., 1986; O'Connor et al., 1984). These changes in the hemostatic system could also explain the rapid decrease in excess risk seen when smoking is stopped (FitzGerald et al., 1988).

Direct hemodynamic responses also occur in response to the release of nicotine during smoking and may further contribute to the development of CHD. Stimulation of the sympathetic nervous system and the adrenal glands result in an acute increase in plasma norepinephrine and epinephrine (Cryer, Haymond, Santiago, & Shah, 1976). Cardiac output and vascular resistance increase, leading to tachycardia and transiently elevated systolic and diastolic blood pressure (Cryer et al., 1976; Mancia et al., 1990; Tachmnes, Fernandez, & Sachner, 1978; Wilhelmsen, 1988). Most epidemiologic studies, however, demonstrate a negative association between smoking and blood pressure (Schoenenberger, 1982; Wilhemsen, 1988). A possible explanation for this phenomenon is that during epidemiologic studies, smokers are usually required to abstain from smoking for at least four hours before the blood pressure is measured. Because the elevation in blood pressure that occurs with smoking is only transient, it was not reflected in these measurements (Mancia et al., 1990; Wilhemsen, 1988).

A direct effect of smoking on the heart was identified by Deanfield et al. (1986) when profound disturbances of regional myocardial perfusion were demonstrated in individuals with coronary artery disease and angina during the smoking of just one cigarette. This finding suggests that smoking impairs the coronary blood supply, possibly resulting in frequent episodes of silent ischemia.

There are obviously many physiologic responses to cigarette smoking that can increase the risk for CHD. The presence of one major risk factor, (smoking, hypertension, or hypercholesterolemia), increases the incidence of CHD by two to four times, while the presence of two factors increases the risk by as much as nine times, and when all three are present, the risk increases by as much as 16 times (Mancia, 1988). This risk increases proportionally with the number of cigarettes smoked, and rapidly decreases when smoking is stopped. Within a few years, the relative risk for both men and women was similar to individuals who had never smoked (Palmer, Rosenberg, & Shapiro, 1989; Rosenberg, Kaufman, Helmrich, Miller et al., 1985a; Rosenberg, Kaufman, Helmrich, & Shapiro, 1985b).

The risk of fatal coronary heart disease or nonfatal MI in women who smoke only one to four cigarettes per day was more than double the risk of nonsmokers (Rosenberg et al., 1985a; Willett et al., 1987). The risk for women who smoke 25 or more cigarettes a day was more than 500% the risk in nonsmokers (Fielding, 1987; Willett et al., 1987). It was estimated that smoking caused more than 80% of the myocardial infarctions among heavy smokers (Willett et al., 1987). Palmer et al. (1989) demonstrated that the increase in risk was just as great for women who smoked the lowest-yield cigarettes.

Coronary heart disease is now the leading cause of excess disability and death among smokers in North America

and Northern Europe (Wilhelmsen, 1988). Cigarette smoking among women is of particularly concern due to the fact that the number of women smokers has declined at a considerably slower rate than the number of male smokers. Since 1964, when the first Surgeon General's report on smoking and health was released, the proportion of American men who smoke had decreased by almost half, from 51% to 29% in 1986, while the proportion of women who smoke had only decreased by less than one third, from 33% to 24% (Rosenberg, Palmer, & Shapiro, 1990). This trend appears to be do to differences in initiation rates. The prevelance of smoking among high school senior girls has exceeded that among boys for over ten years (Fielding, 1987; Fiore et al., 1989). Currently, 25.7% of adult women smoke, compared with 31.5% of men (Fielding, 1987).

Summary

A vast amount of research has been conducted on CHD and the associated risk factors; however, the majority of the studies have focused on men. A primary reason is that the Framingham Heart Study, which began over 40 years ago, initially reported that heart disease was a much bigger problem for men than for women. It is now apparent that just as many women have heart attacks, only women generally have them ten to fifteen years later than men. Subsequently, much of the data about women have been examined retrospectively rather than prospectively.

Some disturbing facts have also come to light in some of the more recent research. Compared to men, women have a greater chance of dying within the first 30 days following a myocardial infarction and are more likely to sustain reinfarction over the following five years (Becker, 1990). In addition, the incidence of congestive heart failure is higher in women (Becker, 1990).

Very little data about risk factors, preventative therapy, and a woman's response to treatment are available. Generally, the results from the research with men has arbitrarily been used to try to prevent, diagnose, and treat CHD in women, even though major physiological differences in the cardiovascular response of men and women have been identified. Identification of risk factors and their interrelations in women are needed to promote the use of the most appropriate screening and diagnostic measures early in the atherosclerotic process when preventative interventions are most successful.

CHAPTER III
METHODOLOGY

This descriptive correlational study was designed to examine the relation between cigarette smoking, distribution of body fat, and density of lipoprotein cholesterol in women. Variables selected for study were total serum cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, exposure to cigarette smoke, and the waist to hip circumference ratio. Additional variables identified as CHD risk factors or that have been shown to influence lipoprotein levels in previous research were also selected for this study and include age, ethnic origin, marital status, work history, family income, education, height, weight, blood pressure, level of physical activity, alcohol consumption, use of oral contraceptives, and a history of hysterectomy, bilateral oopharectomy, menopause, and estrogen therapy.

Setting

This study was conducted in North Florida at the following three sites: 1) the family planning and primary care clinics in a rural, county health department. This population includes a wide range of women of all ages who primarily have an appointment for an annual examination or follow-up for a particular chronic medical problem. 2) a large, independent retirement community with over 8,000

residents. The community is centered around golf and other activities that promote an active and involved lifestyle and 3) a private health and fitness center with individual and group programs that include equipment training, aerobics, swimming, and rehabilitation.

Sample

The total sample consisted of 75 adult women over the age of 18 years. In order to assure representation of women before and after menopause, a wide range of ages were included (22 - 74 years). Data were collected from 55 women at the above mentioned data collection sites. Existing data on 20 subjects over the age of 50 who participated in a separate research study investigating cholesterol and serum lipoprotein levels in women conducted by Dawn O'Byrne, MS, RD were also included.

Exclusion Criteria

The following were exclusion criteria for individuals in this investigation: 1) pregnancy 2) up to three months post-partum and 3) current drug therapy to lower cholesterol.

Instruments

Laboratory Analysis

Lipid and lipoprotein determinations were performed on fresh serum samples collected after at least 12 hours of fasting. Two laboratories were used for analysis:

1) Allied Clinical Lab in St. Petersburg, FL and
2) Laboratory Services at MacDill AFB, FL.

Both laboratories employ a standardization program, therefore accurate and reliable measurements are presumed.

Cholesterol levels were determined by the Abell-Kendall method in both laboratories. Accepted cholesterol values according to the American Heart Association are

Desirable blood cholesterol	< 200 mg/dL
Borderline high cholesterol	200 - 239 mg/dL
High blood cholesterol	≥ 240 mg/dL

High density lipoprotein (HDL)-cholesterol was determined using Cantrol's Dextran Sulfate / Magnesium precipitation at MacDill AFB Laboratory. Split sample comparisons between Cantrol HDL-Cholesterol Precipitating Reagent and the accepted standard, Northwest Lipid Research Clinic's reference method, indicate agreement (Product Information, Canyon Diagnostics Inc, 1992). Allied Clinical Laboratory determined HDL-cholesterol values with an automated device (Olympus Demand) using magnesium chloride as the precipitating reagant. Normal expected values of both methods are similar with an acceptable range of 35-86 mg/dL for women.

Triglycerides were measured using an automated procedure with enzymatic, colormetric methodology at both laboratories. Slight variation in the upper limit considered "normal" is noted: MacDill AFB Laboratory (38 - 162 mg/dL)

Allied Clinical Laboratory (40 - 200mg/dL)

This variation did not affect the analyses for this investigation.

Low density lipoprotein (LDL)-cholesterol is a calculated value estimated from measurements of other lipids, using the following formula:

LDL = Total Cholesterol - HDL-cholesterol - Triglyceride/5

Accuracy of this formula has been demonstrated with triglyceride values under 400 mg/dL (Report of the Expert Panel, 1988). All triglyceride values in this study were under 400 mg/dL.

Questionnaire

A questionnaire developed by the investigator was used to collect sociodemographic data and health status variables in relation to CHD (Rose, 1982). Pertinent health-related behaviors such as a detailed smoking history, alcohol consumption, and physical activity were also included (Appendix A).

Risk Factor Prediction

A Coronary Heart Disease Risk Factor Prediction Worksheet distributed by the American Heart Association was completed for all participants and a risk probability was determined (Appendix B). Left ventricular hypertrophy (LVH) was not evaluated and is presumed to be negative in formulating the risk factor profile. The sensitivity for detecting LVH by electrocardiography (ECG) is poor and according to Grauer (1992), does not exceed 60%, even by experts.

Procedure

Approval was obtained from the University of Florida Health Center Institutional Review Board for collection of

data at all three sites. Permission was also obtained from the director of the health department, director of the resident's ammenities division at the retirement community, and manager of the health and fitness center, prior to data collection.

Request for exemption from institutional review was submitted and approved for use of the existing data on 20 subjects who participated in a separate research study conducted by Dawn O'Byrne, MS, RD. Consent for access to the data was obtained from Dawn O'Byrne, MS, RD. Permission was also obtained from Lieutenant Colonel Sherrell L. Russell, Chief, Laboratory Services at MacDill Air Force Base to have the lipid profiles analyzed in the laboratory at MacDill AFB.

Subjects at the county health department were identified from a computer list of scheduled appointments during the study period. The investigator contacted 29 individuals before their appointment either by telephone or letter to invite them to participate in the study and instruct them to fast for at least 12 hours before their appointment. Five individuals participated.

Subjects were recruited at the retirement community through a newspaper advertisement and television announcement and were instructed to fast for at least 12 hours by the investigator when they called to make an appointment. The majority of the 33 individuals who participated at this site were physically active and very interested in ways to maintain or improve their health.

Subjects were recruited at the health and fitness center through personal announcements to the staff and aerobics classes. Instructions to fast for at least 12 hours were given at the time of the announcement. The seventeen individuals participating at this site were members of the club or staff members.

A questionnaire was used to collect sociodemographic data and health status variables in relation to CHD. Socio-demographic data included age, ethnic origin, marital status, work history, and level of education. Risk factors specific to women such as a history of hysterectomy, oopharectomy, menopause, estrogen replacement therapy, and use of oral contraceptives were also included. Pertinent health-related behaviors that have been shown to influence cholesterol and/or lipoprotein levels and CHD risk, that were included in the questionnaire were cigarette smoking, alcohol consumption, and physical activity.

Clinical data were obtained by the investigator and three assistants. Specific instructions were given to each assistant regarding the measurement protocols to assure accuracy and reliability. Data collection proceeded according to the following steps:

1) Height and weight were measured in light clothing, without shoes, using a standard, calibrated balance scale with a vertical measuring rod. Height was measured to

the nearest quarter inch. Weight was rounded to the nearest pound with 0.5 pounds or more being rounded up to the next higher pound.

2) The waist circumference was measured to the nearest quarter inch with a standard tape measure at a level midway between the lower rib margin and the iliac crest at the smallest part. All subjects were wearing light clothing and were measured in a standing position.

3) The hip circumference was measured to the nearest quarter inch with a standard tape measure at the widest part of the hips over the greater trochanters. All subjects were wearing light clothing and were measured in a standing position.

4) Blood pressure was measured in the left arm with a standard sphygmomanometer and stethescope after the subject rested in the sitting position for at least 2 minutes.

5) Pulse rate was obtained by palpating the radial artery and was counted for at least 15 seconds.

6) A 12-hour fasting, venous blood sample was drawn for the lipid profile using a vacuum tube collection system. The blood sample tubes were refrigerated and centrifuged within six hours with the caps in place. The samples were delivered in a cooler containing ice to the laboratory at MacDill AFB within 48 hours for analysis.

In addition to measuring the variables of interest, an overall coronary heart disease risk factor analysis was completed and sent to each participant. Each subject also

received a copy of her lipid profile results with the desired values and an explaination of what her results could indicate in regard to her risk for developing CHD (Appendix C). The following pamphlets, published by the American Heart Association, were sent to each participant to provide suggestions on how to follow a healthy lifestyle and reduce any risk factors that she can control: 1) Silent Epidemic: The Truth About Women and Heart Disease (AHA, 1989a), 2) Cholesterol and Your Heart (AHA, 1989b), and 3) Smoking and Heart Disease (AHA, 1986). All participants were advised to show the results to their health care providers for follow-up care.

Human Subjects

Informed consent was obtained from each participant prior to data collection (Appendix D). Because data was obtained from the laboratory report and direct measurement and matched to the questionnaire responses, complete anonymity was not possible. However, numbers were assigned to all data for recording purposes to ensure greater confidentiality. All data relating a subject's name to the results was destroyed at the completion of the research.

Statistical Analysis

Correlation analysis utilizing the SAS System was employed to test the research hypotheses. Pearson and Spearman correlation coefficients were calculated for selected variables to quantify the relationships between

variables. Two-tailed probability values of less than 0.05 were considered statistically significant for the purpose of this study. A data collection form was used to help organize the data (Appendix E).

CHAPTER IV
DATA ANALYSIS

The purpose of this study was to describe the relation between cigarette smoking, distribution of body fat, and density of lipoprotein cholesterol in women. The variables studied included total serum cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, exposure to cigarette smoke, and the waist to hip circumference ratio. Additional variables identified as CHD risk factors or that have been shown to influence lipoprotein levels in previous research were also selected for this study and include age, ethnic origin, marital status, work history, family income, education, height, weight, blood pressure, level of physical activity, alcohol consumption, use of oral contraceptives, and a history of hysterectomy, bilateral oopharectomy, menopause, and estrogen therapy.

Sample

The total sample consisted of 75 adult women over the age of 18 years. In order to assure representation of women before and after menopause, a wide range of ages were included (22-74 years). The majority of individuals were white (n = 63; 84%), married (n = 48; 64%), and had at least one child (n = 54; 72%). Slightly over one-half of the

subjects were employed either full- or part-time (n = 38; 51.4%) and approximately one-half of the respondents reported their family income to be over $30,000 per year (n = 33; 51.5%). The subjects' education level ranged from 8 to 19 years with a mean of 14 years. Tables 1 and 2 summarize the sample sociodemographic characteristics.

The participants in this study were physically very active with over 81% reporting some form of regular exercise (n = 61; 81.4%). Over one half reported the average length of each exercise session to be over 30 minutes (n = 38; 50.7%). The majority of individuals reported some alcohol consumption (n = 49; 69%), however very few reported daily usage (n = 4; 5.6%).

Seventy-two participants completed the smoking history portion of the questionnaire. Only 9 women were current cigarette smokers (n = 9; 12.5%) and 4 of these women also live with a smoker. Twenty women were former cigarette smokers (n = 20; 32.3%) with 9 currently living with a smoker. Descriptions of the health-related behavior characteristics are summarized in Table 3.

Fifty-three (70.7%) women had stopped having their menstrual period. Twenty-two (29.3%) had a hysterectomy at a mean age of 42.9 (SD 11.32) years. A bilateral oopharectomy was reported by 9 (12%) women at a mean age of 42.1 (SD 10.25) years. Over one-half of the women who had stopped menstruating reported a natural menopause (n = 33; 62.3%) at a mean age of 45.9 (SD 8.70) years. Two of these women also

Table 1

Frequency and Percent of Sociodemographic Data (n = 75)

Variables	Frequency	Percent
Age		
18 - 30	8	10.7
31 - 40	13	17.3
41 - 50	7	9.3
51 - 60	17	22.7
61 - 70	26	34.7
71 - 80	4	5.3
Ethnic Origin		
White	63	84
Black	9	12
Hispanic	3	4
Marital Status		
Single	15	20
Married	48	64
Widowed	4	5.3
Separated	2	2.7
Divorced	6	8.0
Number of Children		
None	21	28
1	6	8
2	18	24
3	18	24
4	7	9.3
5	4	5.3
6	1	1.3
Work History		
Working Full-time	29	39.2
Working Part-time	9	12.2
Housewife	10	13.5
Unemployed	4	5.4
Disabled	2	2.7
Retired	15	20.3
Student	5	6.8
No Response	1	

Table 1--continued

Variables	Frequency	Percent
Family Income		
Under 5,000	2	3.1
5,000 - 9,999	3	4.7
10,000 - 19,999	14	21.9
20,000 - 29,999	12	18.8
30,000 - 39,999	15	23.4
40,000 - 49,999	7	10.9
50,000 or over	11	17.2
No Response	11	

Table 2

Summary Measures of Age and Education (n = 75)

Variables	Min - Max	Mean	SD
Age (Year) (n = 75)	22 - 74	51.7	14.9
Education (Year) (n = 75)	8 - 19	14.1	2.6

Table 3

Frequency and Percent of Selected Health Related Behaviors

Variable	Frequency	Percent
Physical Activity (n = 75)		
Never	14	18.7
Rarely (Once a week)	8	10.7
Occasionally (Twice a week)	7	9.3
Moderately (Three times a week)	17	22.7
Frequently (More than 3 times a week)	29	38.7
Length of Average Exercise Session (n = 75)		
Never Exercises	14	18.7
Less than 10 Minutes	2	2.7
10 - 20 Minutes	9	12.0
20 - 30 Minutes	12	16.0
Over 30 Minutes	38	50.7
Alcohol Consumption (n = 71)		
Each of the following equals "one drink"		
12 ounces of beer (one can)		
4 ounces of wine (small glass)		
1 cocktail with one "shot" of liquor		
Rarely (1 - 2 drinks per month)	18	25.4
Occasionally (1 drink per week)	12	16.9
Moderately (2 - 5 drinks per week)	15	21.1
Frequently (Daily)	4	5.6
Never	22	31.0
Cigarette Smoking (n = 72)		
Current Smoker	9	12.5
Amount of Cigarette that Burns Without Smoking It:		
Very Little	1	12.5
Some	2	25.0
Moderate Amount	2	25.0
Great Deal	3	37.5
Current Smoker Living with Smoker	4	44.4
Former Smoker	20	32.3
Former Smoker living with Smoker	9	22.5

had a hysterectomy done after menopause. One 26 year old woman stated she had stopped menstruating at the age of 25 due to obesity. Twelve (22.7%) of the women are currently taking estrogen replacement therapy for symptoms of menopause such as hot flashes, vaginal dryness, and osteoporosis. Only nine (12%) women are currently taking oral contraceptives. Tables 4 and 5 summarize the factors specific to women that have been shown to influence cholesterol and/or lipoprotein levels and affect a woman's risk for developing CHD.

Table 4

Frequency and Percent of Factors Specific to Women That Have Been Shown to Influence Cholesterol and/or Lipoprotein Levels and Affect a Woman's Risk for Developing CHD (n = 75)

Variables	Frequency	Percent
Hysterectomy	22	29.3%
Oopharectomy	9	12.0%
Menopause (Total)	53	70.7%
Natural	33	62.3%
Surgical	20	37.7%
Estrogen Replacement Therapy	12	16.0%
Currently Taking Oral Contraceptives	9	12.0%

Table 5

Summary Measures of Age When Menopause, Hysterectomy, and/or Oopharectomy Occurred

Variables	Min - Max	Mean	SD
Menopause Age (Total) Natural & Surgical (Year) (n = 53)	22 - 58	45.9	8.7
Hysterectomy Age (Year) (n = 22)	22 - 65	42.9	11.3
Oopharectomy Age (Year) (n = 9)	25 - 54	42.1	10.3

The summary measures of the selected quantitative variables in this investigation that have been shown to influence cholesterol and/or lipoprotein levels and CHD risk are shown in Table 6. Pulse rate was not available in the existing data from the 20 participants who were included in this study from the separate research project conducted by Dawn O'Byrne MS, RD.

Table 6

Summary Measures for the Selected Quantitative Variables That Have Been Shown to Influence Cholesterol and/or Lipoprotein Levels and CHD Risk

Variables	Min - Max	Mean	SD
Height (Inches) (n = 75)	55.50 - 70.00	63.70	3.24
Weight (Pounds) (n = 75)	95.00 - 352.0	148.90	36.24
Waist Circumference (Inches) (n = 75)	23.75 - 50.00	31.20	5.00
Hip Circumference (Inches) (n = 75)	33.00 - 65.50	40.30	4.66
Waist/Hip Ratio (n = 75)	0.657 - 0.981	0.77	0.06
Systolic Blood Pressure (mmHg) (n = 75)	92 - 148	119	11.38
Diastolic Blood Pressure (mmHg) (n = 75)	60 - 96	77.70	8.52
Pulse Rate (per Minute) (n = 55)	52 - 98	71	9.94
Lipid Profile			
Total Cholesterol (mg/dL) (n = 75)	143 - 323	220	40.72
HDL-cholesterol (mg/dL) (n = 75)	29 - 88	53.80	13.52
LDL-cholesterol (mg/dL) (n = 75)	59 - 219	137	36.85
Cholesterol/HDL Ratio (n = 75)	2.26 - 8.50	4.35	1.40
Triglycerides (mg/dL) (n = 75)	47 - 394	145.60	75.83

Results

Hypothesis One

The hypothesis that cigarette smoking would correlate with an increased waist to hip circumference ratio (apple shape) and decreased HDL-cholesterol was not supported by the study results. There was no significant correlation between cigarette smoking and the waist to hip circumference ratio ($r = -.05$, $p = .6612$), and no significant negative correlation between cigarette smoking and HDL-cholesterol ($r = -.04$, $p = .7615$). There was, however, a significant correlation between cigarette smoking and total cholesterol ($r = .25$; $p = .0309$) and between cigarette smoking and LDL-cholesterol ($r = .31$, $p = .0072$). The number of cigarettes smoked per day showed a significant positive correlation with LDL-cholesterol ($r = .28$, $p = .0275$). A significant negative correlation was also demonstrated between the reported amount of the cigarette that burns without smoking it and the total cholesterol level ($r = -.80$, $p = .0164$) and the LDL-cholesterol level ($r = -.80$, $p = .0164$).

Hypothesis Two

The hypothesis that an increased waist to hip circumference ratio (apple shape) would correlate with decreased HDL-cholesterol, increased triglycerides, and increased total and LDL-cholesterol was partially supported by the study results. There was a significant negative correlation between the waist/hip ratio and HDL-cholesterol ($r = -.37$, $p = .0010$). There was also a significant

positive correlation between the waist/hip ratio and triglycerides ($r = .57$, $p = .0001$). Initially, a significant correlation was demonstrated between the waist/hip ratio and total cholesterol ($r = .25$, $p = .0299$), however, when the correlation was adjusted for age, height, weight, and education, the association was no longer significant ($r = .05$, $p = .6573$). No significant correlation was demonstrated between the waist/hip ratio and LDL-cholesterol ($r = .18$, $p = .1219$). A significant negative correlation was demonstrated between the waist/hip ratio and years of education ($r = -.28$, $p = .0155$). Additional, significant positive correlations were demonstrated between the waist/hip ratio and 1) weight ($r = .38$, $p = .0006$), 2) systolic blood pressure ($r = .32$, $p = .0057$), and 3) diastolic blood pressure ($r = .23$, $p = .0463$).

Summary

This study describes the relation between cigarette smoking, distribution of body fat, and density of lipoprotein cholesterol in women. The first hypothesis statement that cigarette smoking would correlate with an increased waist to hip circumference ratio (apple shape) and decreased HDL-cholesterol was not supported by the study results. No significant correlations were demonstrated between these variables. There was, however, a significant correlation between cigarette smoking and total and LDL-cholesterol.

The second hypothesis statement that an increased waist to hip circumference ratio (apple shape) would correlate with decreased HDL-cholesterol, increased triglycerides, and increased total and LDL-cholesterol was partially supported by the study results. A significant negative correlation was demonstrated between the waist/hip ratio and HDL-cholesterol. A strong correlation was also found between an increased waist/hip ratio and increased triglycerides. The total cholesterol initially showed a significant correlation with the waist/hip ratio, however, when controlling for age, height, weight, and level of education, the correlation was no longer significant. Low density lipoprotein (LDL)-cholesterol also was not significantly correlated with an increased waist to hip circumference ratio (apple shape). Other variables that demonstrated a significant positive correlation with the waist to hip circumference ratio were weight, systolic, and diastolic blood pressure.

CHAPTER V
DISCUSSION, IMPLICATIONS, AND RECOMMENDATIONS

Discussion of Results

The purpose of this research was to describe the relation between cigarette smoking, distribution of body fat, and density of lipoprotein cholesterol in women. The variables selected for study have been identified as risk factors for developing CHD or have been shown to influence lipoprotein levels in previous research and have the potential to be modified through lifestyle changes. The variables studied included total serum cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, exposure to cigarette smoke, and the waist to hip circumference ratio. Correlation between these variables has been demonstrated in some previous studies and a synergistic effect is seen when two or more of these risk factors are present as far as developing heart disease is concerned. However, because most of the research that identified risk factors and subsequently evaluated the effectiveness of interventions designed to modify them was done with men, it remains uncertain whether the weight of risk factors and their interrelations are the same among women.

The findings from this study did not demonstrate a significant correlation between cigarette smoking and body

fat distribution as measured by the waist to hip circumference ratio or between cigarette smoking and HDL-cholesterol. Results reported in most of the literature have indicated that plasma HDL-cholesterol levels tend to be lower in men and women smokers than in nonsmokers. Criqui et al., (1980) examined 2663 men and 2553 women in 10 North American populations, adjusting for differences between smokers and nonsmokers in age, obesity, alcohol consumption, exercise and gonadal hormone use, and found that cigarette smoking was associated with substantially lower levels of HDL-cholesterol. This association appeared to be dose-dependent and consistent with other research, indicating a possible causal relationship between cigarette smoking and lower HDL-cholesterol. Similarly, Garrison et al., (1978) found a consistent inverse association between cigarette smoking and HDL level in a group of 2149 women and 1958 men from the Framingham Heart Study. Mjos (1988) examined plasma lipid levels in men and also found smoking lowers the HDL-cholesterol level by an unknown mechanism.

Only nine (12.5%) women in this investigation were current smokers. The small sample size is one possible explanation for the lack of a negative correlation between cigarette smoking and HDL-cholesterol evident in this study. A much larger population of smokers was initially expected in the study sample. A very low response rate from the county health department and the fact that only 26 subjects were

younger than 50 years of age may account for the fact that only 12.5% of the respondents were current cigarette smokers. Most of the data indicate that younger women (20-24 years of age) comprise the group that has been increasing their cigarette use (Leaf, 1988). DuNah, Holly, & Ahn (1991) reported that women with fewer years of education smoked more cigarettes per day than women who were more educated.

There was a significant positive correlation demonstrated between smoking and total cholesterol and LDL-cholesterol. Mjos (1988) reported that no significant differences in total cholesterol and triglycerides were found between heavy smokers and nonsmokers. Memmer (1989) stated that tobacco smoke has been shown to increase LDL-cholesterol in smokers, possibly due to the nicotine stimulating adrenergic activity, which in turn, stimulates a rise in LDL-cholesterol levels. Because 70% of the total cholesterol level is attributed to LDL-cholesterol, any increase in LDL levels will also result in an increased total cholesterol level.

A significant positive correlation between cigarette smoking and the waist/hip circumference ratio has been demonstrated in most studies. Marti, Tuomilehto, Salomaa, Kartovaara, Korhonen, & Pietinen (1990) conducted a study of 2526 men and 2756 women in Finland and found a significant positive correlation between cigarette smoking and abdominal obesity as measured by the waist/hip circumference ratio. Selby, Newman, Quesenberry, Fabsitz, Carmelli, Meaney, &

Slemenda (1990) examined 265 pairs of male twins and also reported that cigarette smoking was strongly related to the waist/hip circumference ratio. The results from this investigation did not support these findings, however, the very small sample size could account for the variation.

A significant negative correlation was demonstrated between the waist to hip circumference ratio and HDL-cholesterol in this study. This finding is consistent with the majority of research and could account for some of the increased risk for developing CHD that has been related to this type of body fat distribution (apple shape). Despres et al., (1990) further studied the associations between obesity, body fat distribution, and serum HDL-cholesterol levels in a sample of 429 men and demonstrated that the effect of obesity on serum HDL-cholesterol levels was no longer significant after controlling for abdominal fat depositon. These results indicate that the association between obesity and serum HDL-cholesterol levels previously reported was mainly explained by the amount of abdominal fat.

Anderson et al., (1988), studied 713 men and 520 women who were apparently healthy in order to assess the relation of the waist/hip ratio to plasma lipoproteins in persons who were not necessarily overweight. This population also demonstrated an inverse association between the waist/hip ratio and HDL-cholesterol, even after controlling for age, alcohol intake, exercise level, current smoking status, and oral contraceptive use.

The waist/hip ratio has also consistently shown a positive correlation with levels of total cholesterol, LDL-cholesterol, and triglycerides. Zwiauer, Widhalm & Kerbl (1990) found this correlation in a group of 74 grossly obese adolescents. Similar findings were reported in 1,233 apparently healthy men and women by Anderson et al. (1988). Despres et al. (1990) cited studies that indicate in premenopausal women, obesity has to be present for there to be significant associations between intra-abdominal fat accumulaton and plasma lipoprotein concentrations. Lean women showed little association between the waist/hip ratio and lipoprotein levels.

The results from this investigation did not demonstrate a significant correlation between the waist/hip ratio and total cholesterol or LDL-cholesterol, however, the mean weight for the participants in this study was only 148.9 pounds (SD 36.24). Triglycerides, however, were positively associated with the waist/hip ratio.

In summary, many of the correlations between cigarette smoking, body fat distribution, and density of lipoprotein cholesterol in the 75 apparently healthy women who participated in this investigation were not statistically significant. The only significant correlations found were between an increased waist to hip circumference ratio and decreased HDL-cholesterol levels and between an increased waist/hip ratio and increased triglyceride levels. In contrast, the preponderance of scientific studies have found

significant correlations between cigarette smoking and the waist/hip ratio and HDL-cholesterol levels as well as between the waist/hip ratio and total cholesterol, HDL-cholesterol, LDL-cholesterol, and triglyceride levels. These findings illustrate the complex interrelations between body fat distribution, serum levels of lipids and lipoproteins, and the many variables that have been identified as CHD risk factors. While statistical models provide objective ways to evaluate associations between variables, they may tend to oversimplify the complex biological processes involved in lipid metabolism, lipoprotein transport, and the distribution of body fat and should be interpreted with caution. This study primarily used simple statistics to investigate the relationship between the variables of interest. The majority of the correlational studies have used some type of multivariate technique in order to take the intercorrelations of the variables into account. Another important fact to consider in comparing the results of this study is the small number of participants who are current cigarette smokers. The small sample size limits any meaningful interpretation of these results.

Implications

The results from this study illustrate how conflicting results are often encountered when investigating the correlation between risk factors for CHD. Risk factors have been studied for over 40 years and a great deal of controversy still exists over how these factors actually

influence a person's risk for developing heart disease. Because so many of the variables reflect complex biological processes and are closely interrelated, statistical models used for analysis need to be as uniform as possible in order to compare the results from different studies in a meaningful way.

Very few prospective studies have included women which has limited our understanding of gender-related differences in CHD risk factors, clinical manifestations, and a woman's response to treatment and recommended preventative measures. Because women generally do not develop symptomatic CHD until after the age of 50, they were thought to be protected and preventative measures were largely ignored until manifestations of heart disease were clinically evident. Risk factor modifications were then recommended, however, these were based on research predominantly done with men. Unfortunately, by the time symptoms develop, the disease process is more advanced and the effectiveness of risk factor modifications is reduced.

The "sexual bias" in cardiology is a major barrier to the investigation and prevention of heart disease in women. Finding a population of women for this particular study, who were basically healthy and having a lipid profile done for CHD risk factor analysis was extremely difficult. Screening for total cholesterol levels was common, but a lipid profile was rarely ordered for women unless the total cholesterol

level was significantly elevated. Ironically, a large number of men were having lipid profiles done for CHD risk factor analysis.

Some of the major implications for nursing practice are awareness and education. Changing life styles to decrease risk for developing heart disease is as important for women as it is for men. These changes need to be started early to delay or prevent the progression of the disease. Cigarette smoking, diet modification, weight control, and exercise are all areas that need an increased emphasis in women. In addition, all women should have their lipid profile evaluated in order to identify those at high risk and to target intervention strategies for effective risk reduction.

Recognizing that women often have different responses to CHD and its treatment will enable the clinical nurse to plan more effective, individualized care for their women patients undergoing diagnostic testing and/or recovering from a CHD related incident.

Recommendations for Future Research

The results currently available from previous research regarding CHD risk factors have shown that differences do exist between men and women in how CHD develops and responds to preventative measures. Risk factors specific to women such as menopause, estrogen replacement therapy, and use of oral contraceptives have also been shown to influence a woman's risk for developing heart disease. The precise mechanisms

responsible for these relationships are unknown. Additional studies are needed to investigate the relationship between any of the risk factors in women.

Further research is also needed to distinguish between physiological and environmental influences of CHD in women, particularly prospective studies. Replication of this study using two groups (current cigarette smokers and non-smokers) for comparison would provide more specific information regarding the influence of smoking on the other risk factor variables. Research involving a woman's response to CHD is also needed to determine the most appropriate medical and nursing interventions for women with CHD.

In summary, research investigating CHD in women is just beginning and almost any area related to risk factors and CHD warrants further investigation. Of particular interest are those risk factors that are modifiable, such as cigarette smoking and elevated lipid and lipoprotein levels, because they have the greatest potential to make a difference in overall morbidity, mortality, and health care expenditures.

APPENDIX A
SOCIODEMOGRAPHIC QUESTIONNAIRE

Study Number_____

Age_____ Ethnic Origin: ☐ White
☐ Black
☐ Hispanic
☐ Oriental
Other_____

Marital Status: ☐ Single (Never Married)
☐ Married
☐ Widowed
☐ Separated
☐ Divorced
☐ Living as married

Number of Children: _____

Work History: (Check all that apply)

☐ Working full-time
☐ Working part-time
☐ Housewife
☐ Unemployed
☐ Disabled
☐ Retired
☐ Sick Leave
☐ Student

Annual Income of your Family:

☐ Under 5,000
☐ 5,000 - 9,999
☐ 10,000 - 19,999
☐ 20,000 - 29,999
☐ 30,000 - 39,999
☐ 40,000 - 49,999
☐ 50,000 or over

Education: Circle Highest Grade Completed

0 1 2 3 4 5 6 7 8 9 10 11 12

College: 1 2 3 4

Graduate School: 1 2 3 4

Physical Activity: How often do you exercise?

☐ Never
☐ Rarely (once a week)
☐ Occasionally (twice a week)
☐ Moderately (three times a week)
☐ Frequently (more than three times a week)

How long does each of your exercise sessions last?

- ☐ I never exercise
- ☐ Less than 10 minutes
- ☐ 10 - 20 minutes
- ☐ 20 - 30 minutes
- ☐ Over 30 minutes

MEDICAL HISTORY

Have you ever had:

	Yes	No
Diabetes (sugar disease)	☐	☐
Stroke	☐	☐

	Yes	No
Did a doctor ever tell you that you had heart trouble?	☐	☐

If yes, what did he call it _____

What was your age? _____

	Yes	No
Have you ever taken any medicine for heart trouble?	☐	☐

	Yes	No
Did a doctor ever tell you that you had high blood pressure?	☐	☐

What was your age? _____

	Yes	No
Have you ever taken any medicine for high blood pressure?	☐	☐

Have you had a hysterectomy? (uterus or womb surgically removed) ☐ Yes ☐ No

At what age? _____

Have you had both ovaries surgically removed? ☐ Yes ☐ No

At what age? _____

Have you stopped having your menstrual period? ☐ Yes ☐ No

At what age? _____

Are you currently taking hormones for symptoms of menopause such as hot flashes, vaginal dryness, and bone thinning? (Estrogen replacement therapy such as Premarin or Estraderm patch) ☐ Yes ☐ No

Are you currently taking birth control pills (oral contraceptives)? ☐ Yes ☐ No

How long have you been taking the pill?

_____ Years _____ Months ☐ Less than one month

	Yes	No
Do you ever take aspirin?	☐	☐

How many aspirin tablets do you usually take?
- ☐ Less than one per week
- ☐ one to six per week
- ☐ seven or more per week

	Yes	No
Do you take "bulk" laxatives such as Metamucil?	☐	☐

How often?
- ☐ Less than once a week
- ☐ One to three times per week
- ☐ Three to six times per week
- ☐ Every day

	Yes	No
Do you take daily multiple vitamins or niacin?	☐	☐

What brand of vitamins do you take? _____

Which of the following responses best describes your use of alcohol? Each of the following equals one unit of alcohol or "one drink":

12 ounces of beer (one can)
4 ounces of wine (small glass)
1 cocktail with one ounce ("shot") of hard liquor

- ☐ Rarely (1-2 drinks per month)
- ☐ Occasionally (1 drink per week)
- ☐ Moderately (2-5 drinks per week)
- ☐ Frequently (Daily)
- ☐ Never

Do you smoke cigarettes now?

☐ Yes
(If "YES" answer this side)

On the average, about how many cigarettes do you now smoke a day? (1 pack = 20 cigarettes)

_____

How old were you when you began to smoke cigarettes?

_____ Age

How much of your cigarette burns without you smoking it?

- ☐ Very little
- ☐ Some
- ☐ A moderate amount
- ☐ A great deal

What brand of cigarettes do you usually smoke?

_____

Do you live with someone who smokes cigarettes regularly?

☐ Yes ☐ No

If you answered "YES", about how many cigarettes do they now smoke a day?
(1 pack = 20 cigarettes)

_____

☐ No
(If "NO" answer this side)

Have you ever smoked cigarettes regularly in the past?

☐ Yes ☐ No

On average, how many cigarettes per day did you smoke when you last smoked regularly?
(1 pack = 20 cigarettes)

_____

How old were you when you last smoked regularly?

_____ Age

How old were you when you first started to smoke regularly?

_____ Age

Do you live with someone who smokes cigarettes regularly?

☐ Yes ☐ No

If you answered "YES", about how many cigarettes do they now smoke a day?
(1 Pack = 20 cigarettes)

_____

APPENDIX B
RISK FACTOR PREDICTION WORKSHEET

Risk Factor Prediction Worksheet

American Heart Association

1. CORONARY HEART DISEASE — Sum Points For All Risk Factors

_____ (Age) + _____ (HDL-C) + _____ (Total-C) + _____ (SBP) + _____ (Smoker) + _____ (Diabetes) + _____ (ECG-LVH) = _____ (Point Total)

NOTE: *Minus Points Subtract From Total.*

2. Look Up Risk Corresponding To Point Total

Probability			Probability			Probability			Probability		
Pts.	5 Yr.	10 Yr.	Pts.	5 Yr.	10 Yr.	Pts.	5 Yr.	10 Yr.	Pts.	5 Yr.	10 Yr.
≤1	<1%	<2%	9	2%	5%	17	6%	13%	25	14%	27%
2	1%	2%	10	2%	6%	18	7%	14%	26	16%	29%
3	1%	2%	11	3%	6%	19	8%	16%	27	17%	31%
4	1%	2%	12	3%	7%	20	8%	18%	28	19%	33%
5	1%	3%	13	3%	8%	21	9%	19%	29	20%	36%
6	1%	3%	14	4%	9%	22	11%	21%	30	22%	38%
7	1%	4%	15	5%	10%	23	12%	23%	31	24%	40%
8	2%	4%	16	5%	12%	24	13%	25%	32	25%	42%

3. Compare To Average 10 Year Risk

Probability		
Age	Women	Men
30–34	<1%	3%
35–39	<1%	5%
40–44	2%	6%
45–49	5%	10%
50–54	8%	14%
55–59	12%	16%
60–64	13%	21%
65–69	9%	30%
70–74	12%	24%

1. STROKE — Sum Points For All Risk Factors

_____ (Age) + _____ (SBP) + _____ (HYP RX) + _____ (Diabetes) + _____ (CIGS) + _____ (CVD) + _____ (AF) + _____ (LVH) = _____ (Point Total)

2. Look Up Risk Corresponding To Point Total

Men 10 Yr.						Women 10 Yr.					
Pts.	Prob.	Pts.	Prob.	Pts.	Prob.	Pts.	Prob.	Pts.	Prob.	Pts.	Prob.
1	2.6%	11	11.2%	21	41.7%	1	1.1%	11	7.6%	21	43.4%
2	3.0%	12	12.9%	22	46.6%	2	1.3%	12	9.2%	22	50.0%
3	3.5%	13	14.8%	23	51.8%	3	1.6%	13	11.1%	23	57.0%
4	4.0%	14	17.0%	24	57.3%	4	2.0%	14	13.3%	24	64.2%
5	4.7%	15	19.5%	25	62.8%	5	2.4%	15	16.0%	25	71.4%
6	5.4%	16	22.4%	26	68.4%	6	2.9%	16	19.1%	26	78.2%
7	6.3%	17	25.5%	27	73.8%	7	3.5%	17	22.8%	27	84.4%
8	7.3%	18	29.0%	28	79.0%	8	4.3%	18	27.0%		
9	8.4%	19	32.9%	29	83.7%	9	5.2%	19	31.9%		
10	9.7%	20	37.1%	30	87.9%	10	6.3%	20	37.3%		

3. Compare To Average 10-Year Risk

Avg. 10 Yr. Prob. By Age			
Men		Women	
55–59	5.9%	55–59	3.0%
60–64	7.8%	60–64	4.7%
65–69	11.0%	65–69	7.2%
70–74	13.7%	70–74	10.9%
75–79	18.0%	75–79	15.5%
80–84	22.3%	80–84	23.9%

Patient's Name _____ Date _____ Current Point Total _____

Patient's Goal _____ Date of Next Visit _____

May be photocopied as needed

APPENDIX C
LETTER TO PARTICIPANTS

Linda R. Beson RN, BSN
Graduate Student
College of Nursing
University of Florida
Gainesville, FL 32611

23 June, 1992

Dear:

Thank-you for participating in my research study about heart disease risk factors in women.

The results of your Lipid Profile are as follows:

Total Cholesterol (mg/dL) - 223

HDL Cholesterol (mg/dL) - 75

Cholesterol / HDL Ratio - 2.97

LDL Cholesterol (mg/dL) - 132

Triglycerides (mg/dL) - 78

Following are the **Expected Ranges** for these tests:

Total Cholesterol:

Desirable Blood Cholesterol	**<200 mg/dL**
Borderline High Cholesterol	200 - 239 mg/dL
High Blood Cholesterol	≥ 240 mg/dL

HDL-Cholesterol (Women): 35 - 86 mg/dL

Coronary Risk Range Associated With HDL-Cholesterol

Dangerous Level	< 25 mg/dL
High Risk	25 - 34 mg/dL
Moderate Risk	35 - 44 mg/dL
Average Risk	**45 - 54 mg/dL**
Low Risk	55 - 74 mg/dL
Longevity	> 75 mg/dL

Cholesterol / HDL-Cholesterol Risk Factors

Risk	Ratio
1/2 Average Risk	3.3
Average Risk	**4.5**
2 X Average Risk	7.1
3 X Average Risk	11.0

LDL-Cholesterol:

Desirable LDL-Cholesterol	**< 130 mg/dL**
Borderline high-risk LDL	130-159 mg/dL
High-risk LDL	≥ 160 mg/dL

Triglycerides:	38 - 162 mg/dL
Increased risk	> 250 mg/dL

The results of **your** lipid profile:

Are generally within a normal range. Your total cholesterol seems higher than desired, but your HDL-cholesterol (good cholesterol) is very high which lowers your risk. Your LDL-cholesterol is borderline high. Follow a healthy lifestyle and work to reduce any risk factors you can control as recommended in the American Heart Association's pamphlets. Show these results to your health care provider for follow-up care. You should have your cholesterol re-checked within 5-Years.

A number of risk factors have been found to be associated with an increased risk of heart disease. Although most research has been done on men, it is apparent that many of the same risk factors that lead to heart attacks in men also place women at greater risk. Examples of some risk factors are: cigarette smoking, high levels of cholesterol in the blood, high blood pressure, and being overweight.

Attached is a copy of your Coronary Risk Factor Prediction Worksheet published by the American Heart Association. This worksheet estimates the probability that you may develop heart disease over the next 5- to 10-Years in chances per 100. This "average" risk in **not** an optimal risk since it represents the general American population with its high incidence of heart disease. Compared to the **average** 10-year risk given for a woman in the same age category, **your** overall risk is <u>low</u>.

It is <u>very important</u> to keep in mind that your electrocardiogram (ECG) was **NOT** considered in this risk profile. A zero value was given, presuming that you do not have Left Ventricular Hypertrophy (LVH), a condition in which your heart muscle thickens, often in response to high blood pressure. The occurrence of LVH is very rare in younger women (under age 50). If you have left ventricular hypertrophy (seen on ECG), your risk value will increase significantly. Check with your physician to find out if you have this condition.

Fortunately, many risk factors can be modified to lower your chances of getting heart disease. It is now clear that women of all ages should adopt a lifestyle that is healthy for their hearts to protect themselves against this number one killer of women.

If you have any questions about this research or your results, feel free to contact me at (904) 753-8301. Thank-you again for participating in the study.

Sincerely,

Linda R. Beson RN, BSN

APPENDIX D

INFORMED CONSENT TO PARTICIPATE IN RESEARCH

J. Hillis Miller Health Center
University of Florida
Gainesville, Florida 32610

You are being asked to participate in a research study. This form is designed to provide you with information about this study and to answer any of your questions.

1. TITLE OF RESEARCH STUDY

Relation Between Cigarette Smoking, Body Fat Distribution, and Density of Lipoprotein Cholesterol in Women.

2. PRINCIPAL INVESTIGATOR

Linda R. Beson, BSN, RN Graduate Student,
College of Nursing (904) 753-8301

3. THE PURPOSE OF THE RESEARCH

Heart disease is the number one killer of American women, causing 250,000 deaths every year. Research has shown that people with certain traits (called "risk factors") have a greater chance of getting heart disease. Examples of some risk factors are: cigarette smoking, high cholesterol (fat) in the blood, high blood pressure, and being overweight. Most research has been done on men and it is not clear if these risk factors affect women the same way they do men. The purpose of this research is to look at how cigarette smoking, cholesterol levels, and body fat distribution are related in women.

4. PROCEDURES FOR THIS RESEARCH

If you participate, I will need to get the following measurements: 1) height 2) weight 3) blood pressure 4) pulse rate and 5) waist and hip sizes using a regular tape measure. A venipuncture (needle stick) will be necessary to collect one 10 ml. tube of blood (1-1/2 to 2 teaspoonsful). You will also be asked to fill out a short questionnaire (takes about 5 minutes) and return it to me. The questions will ask about some risk factors that may affect your chance of getting heart disease, such as your age, how much you exercise, your medical history, and your exposure to cigarette smoke. I will assign a number to the returned questionnaire and the measurements I do, and your name will not be used.

5. POTENTIAL RISKS OR DISCOMFORTS

The risks of drawing blood from a vein include discomfort at the site of injection; possible bruising and swelling around the injection site; rarely an infection; and, uncommonly, faintness from the procedure. There are no other risks associated with the study. If you wish to discuss these or any other discomforts you may experience, you may call the Project Director listed in #2 of this form.

6. POTENTIAL BENEFITS TO YOU OR TO OTHERS

You may have a chance to know more about heart disease risk factors and what the estimated probability is that <u>you</u> might develop heart disease over the next 5- to 10-years. You will also receive written information, printed by the American Heart Association, about heart disease risk factors for women and how to lessen the risk.

7. ALTERNATIVE TREATMENT OR PROCEDURES, IF APPLICABLE

None.

8. GENERAL CONDITIONS

I understand that I will not receive money for my participation in this study. I understand that I will not be charged additional expenses for my participation in this study. I understand that I am free to withdraw my consent and discontinue participation in this research project at any time without this decision affecting my medical care. If I have any questions regarding my rights as a subject, I may phone (904) 392-3063. In the event of my sustaining a physical injury which is proximately caused by this experiment, Professional Nursing Consultation will be provided me without charge. It is understood that no form of compensation exists other than those described above. I also understand that the University of Florida will protect the confidentiality of my records to the extent provided by law.

9. SIGNATURES

I have fully explained to _____ the nature and purpose of the above-described procedure and the benefits and risks that are involved in its performance. I have answered and will answer all questions to the best of my ability. I may be contacted at telephone number (904) 753-8301

_____ _____

Signature of Principal Investigator Obtaining Consent — Date

I have been fully informed of the above-described procedure with its possible benefits and risks and I have received a copy of this description. I have given permission of my participation in this study.

_____ _____

Signature of Patient or Subject — Date

_____ _____

Signature of Witness — Date

APPENDIX E
DATA COLLECTION FORM

Study Number	Date	Age	Height (Ins.)	Weight (lbs.)	B/P	Pulse	Waist (Ins.)	Hip (Ins.)	W/H Ratio	Total Chol.	HDL (mg/dL)	LDL (mg/dL)	Trig. (mg/dL)	Chol/HDL Ratio

REFERENCES

Addis, P. B., & Warner, G. J. (1991). The potential health aspects of lipid oxidation products in food. In O. I. Aruoma & B. Halliwell (Eds.), Free radicals and food additives (pp. 77-119). London: Taylor and Francis Ltd.

American Heart Association (AHA). (1986). Smoking and heart disease. Dallas, TX: Author.

American Heart Association (AHA). (1988). An older person's guide to cardiovascular health. Dallas, TX: Author.

American Heart Association (AHA). (1989a). Silent epidemic: The truth about women and heart disease. Dallas, TX: Author.

American Heart Association (AHA). (1989b). Cholesterol and your heart. Dallas, TX: Author.

Anderson, A. J., Sobocinski, K. A., Freedman, D. S., Barboriak, J. J., Rimm, A. A., & Gruchow, H. W. (1988). Body fat distribution, plasma lipids, and lipoproteins. Arteriosclerosis, 8(1), 88-93.

Anderson, K. M., Wilson, P. W., Odell, P. M., & Kannel, W. B. (1991). An updated coronary risk profile: A statement for health professionals. Circulation, 83(1), 356-362.

Arntzenius, A. C., Kromhout, D., Barth, J. D., Reiber, J. H. C., Bruschke, V. G., Buis, B., vanGent, C. M., Kempen-Voogd, N., Strikwerda, S., & vanderVelde, E. A. (1985). Diet, lipoproteins, and the progression of coronary atherosclerosis: The Lerdin Intervention Trial. New England Journal of Medicine, 312(13), 805-811.

Auerbach, O., Hammond, E. C., & Garfinkel, L. (1965). Smoking in relation to atherosclerosis of the coronary arteries. New England Journal of Medicine, 273(15), 775-779.

Austin, M. A. (1989). Plasma triglyceride as a risk factor for coronary heart disease. American Journal of Epidemiology, 129(2), 249-259.

Austin, M. A. (1991). Plasma triglyceride and coronary heart disease. Arteriosclerosis and Thrombosis, 11(1), 2-14.

Barret-Connor, E., & Wingard, D. L. (1983). Sex differential in ischemic heart disease mortality in diabetics: A prospective population-based study. American Journal of Epidemiology, 118(4), 489-496.

Becker, R. C. (1990). Introductory article for cardiovascular disease in women. Cardiology, 77(Suppl. 2), 1-5.

Blankenhorn, D. M., Nessim, S. A., Johnson, R. L., Sanmarco, M. E., Azen, S. P., & Cashin-Hemphill, L. (1987). Beneficial effects of combined colestipol-niacin therapy on coronary atherosclerosis and coronary venous bypass grafts. Journal of the American Medical Association, 257(23), 3233-3240.

Brand, R. J., Rosenmon, R. H., Sholtz, R. I., & Friedman, M. (1976). Multivariate prediction of coronary heart disease in the Western Collaborative Group Study compared to the findings of the Framingham Study. Circulation, 53(2), 348-355.

Bray, G. A., & Gray, D. S. (1988). Obesity--Part I: pathogenesis. Western Journal of Medicine, 149(4), 429-441.

Castelli, W. P. (1986). The triglyceride issue: A view from Framingham. American Heart Journal, 112(2), 432-437.

Castelli, W. P., Dawber, T., Feinleib, M., Garrison, R. J., McNamara, P. M., & Kannel, W. B. (1981). The filter cigarette and coronary heart disease: The Framingham Study. Lancet, 2, 109-113.

Castelli, W. P., Garrison, R. J., Wilson, P. W. F., Abbott, R. D., Kalousdian, S., & Kannel, W. B. (1986). Incidence of coronary heart disease and lipoprotein cholesterol levels: The Framingham Study. Journal of the American Medical Association, 256(20), 2835-2838.

Chaitman, B., Bourassa, M. G., Davis, K., Rogers, W. J., Tyras, D. H., Berger, R., Kennedy, J. W., Fisher, L., Judkins, M. P., Mock, M. B., & Killip, T. (1981). Angiographic prevalence of high risk coronary artery disease in patient subsets (CASS). Circulation, 64(2), 360-367.

Clarkson, T. B. (1987). Pathophysiologic processes of atherogenesis. In E. D. Eaker, B. Packard, N. K. Wenger, T. B. Clarkson, & H. A. Tyroler (Eds.), Coronary heart disease in women: Proceedings of an N.I.H. workshop (pp. 11-19). New York: Haymarket Doyma.

Coronary Drug Project Research Group. (1975). Clofibrate and niacin in coronary heart disease. Journal of the American Medical Association, 231(4), 360-381.

Corrao, J. M., Becker, R. C., Ockene, I. S., & Hamilton, G. A. (1990). Coronary heart disease risk factors in women. Cardiology, 77(Suppl. 2), 8-24.

Cotran, R. S., Kumar, V., & Robbins, S. (1989). Robbins pathologic basis of disease (4th ed.). Philadelphia: W. B. Saunders Co.

Criqui, M. H. (1991). Triglycerides and coronary heart disease. Atherosclerosis Review, 22, 75-79.

Criqui, M. H., Wallace, R. B., Heiss, G., Mishkel, M., Schonfeld, G., & Jones, G. T. L. (1980). Cigarette smoking and plasma high-density lipoprotein cholesterol. Circulation (Suppl. 4), 62(4), 70-76.

Cryer, P. E., Haymond, M. W., Santiago, J. W., & Shah, S. D. (1976). Norepinephrine and epinephrine release and adrenergic mediation of smoking associated hemodynamic and metabolic events. New England Journal of Medicine, 295(11), 573-577.

Dawber, T. R., & Meadors, G. F. (1951). Epidemiologic approaches to heart disease: The Framingham Study. American Journal of Public Health, 41(1), 279-286.

Deanfield, J. E., Shea, M. J., Wilson, R. A., Horlock, P., deLandsheere, C. M., & Selwyn, A. P. (1986). Direct effects of smoking on the heart: Silent ischemic disturbances of coronary flow. The American Journal of Cardiology, 57(13), 1005-1009.

Despres, J. P., Moorjani, S., Lupien, P. J., Tremblay, A. N., & Bouchard, C. (1990). Regional distribution of body fat, plasma lipoproteins, and cardiovascular disease. Arteriosclerosis, 10(4), 497-511.

Douglas, P. S. (1986). Gender, cardiology, and optimal medical care [Editorial]. Circulation, 74(5), 917-919.

Doyle, K. T., Dawber, T. R., Kannel, W. B., Kinch, S. A., & Kahn, H. A. (1964). The relationship of cigarette smokingto coronary heart disease. Journal of the American Medical Association, 190(10), 886-890.

DuNah, R. E., Holly, E. A., & Ahn, D. K. (1991). Demographics and cigarette smoking among women. Preventive Medicine, 20, 262-270.

Eaker, E. D., & Castelli, W. P. (1987). Coronary heart disease and its risk factors among women in the Framingham Study. In E. D. Eaker, B. Packard, N. K. Wenger, T. B. Clarkson, & H. A. Tyroler (Eds.), Coronary heart disease in women: Proceedings of an N.I.H. workshop (pp. 122-130). New York: Haymarket Doyma.

Eaker, E. D., Packard, B., Wenger, N. K., Clarkson, T. B., & Tyroler, H. A. (Eds.). (1987). Coronary heart disease in women: Proceedings of an N.I.H. workshop. New York: Haymarket Doyma.

Epstein, F. H. (1987). Commentary: Epidemiologic studies of fatal and non fatal coronary heart disease in women. In E. D. Eaker, B. Packard, N. K. Wenger, T. B. Clarkson, & H. A. Tyroler (Eds.), Coronary heart disease in women: Proceedings of an N.I.H. workshop (pp. 7-10). New York: Haymarket Doyma.

Fielding, J. E. (1987). Smoking and women: Tragedy of the majority. New England Journal of Medicine, 317(21), 1343-1345.

Fiore, M. C., Novotny, T. E., Pierce, J. P., Hatziandreu, E. J., Patel, K. M., & Davis, R. M. (1989). Trends in cigarette smoking in the United States: The changing influence of gender and race. Journal of the American Medical Association, 261(1). 49-55.

FitzGerald, G. A., Oates, J. A., & Nowak, J. (1988). Cigarette smoking and hemostatic function. American Heart Journal, 115(1), 267-271.

Freedman, D. S., Gruchow, H. W., Anderson, A. J., Rimm, A. A., & Barboriak, J. J. (1988). Relation of triglyceride levels to coronary artery disease: The Milwaukee Cardiovascular Data Registry. American Journal of Epidemiology, 127(6), 1118-1130.

Freedman, D. S., Jacobsen, S. J., Barboriak, J. J., Sobocinski, K. A., Anderson, A. J., Kissebah, A. H., Sasse, E. A., & Gruchow, H. W. (1990). Body fat distribution and male/female differences in lipids and lipoproteins. Circulation, 81(5), 1498-1506.

Garrison, R. J., Kannel, W. B., Feinleib, M., Castelli, W. P., McNamara, P. M., & Padgett, S. J. (1978). Cigarette smoking and HDL cholesterol: The Framingham Offspring Study. Atherosclerosis, 30, 17-25.

Godsland, J. F., Wynn, V., Crook, D., & Miller, N. E. (1987). Sex, plasma lipoproteins, and atherosclerosis: Prevailing assumptions and outstanding questions. American Heart Journal, 114(6), 1467-1503.

Goldman, L., & Cook, E. F. (1984). The decline in ischemic heart disease mortality rates. Annals of Internal Medicine, 101(6), 825-836.

Goldstein, J. L., Hazzard, W. R., Schrott, H. G., Bierman, E. L., & Motulsky, A. G. (1973). Hyperlipidemia in coronary heart disease: Lipid levels in 500 survivors of myocardial infarction. Journal of Clinical Investigation, 52(7), 1533-1543.

Gordon, T., Castelli, W. P., Hjortland, M. C., Kannel, W. B., & Dawber, T. R. (1977). High-density lipoprotein as a protective factor against coronary heart disease: The Framingham Study. American Journal of Medicine, 62(5), 707-714.

Gordon, D. J., Probstfield, J. L., Garrison, R. J., Neaton, J. D., Castelli, W. P., Knoke, J. D., Jacobs, D. R., Bangdiwala, S., & Tyroler, H. A. (1981). High-density lipoprotein cholesterol and cardiovascular disease: Four prospective American studies. Circulation, 79(1), 8-15.

Gordon, D. J., & Rifkind, B. M. (1989). High-density lipoprotein--The clinical implications of recent studies. New England Journal of Medicine, 321(19), 1311-1316.

Grauer, K. (1992). A practical guide to ECG interpretation. St Louis, MO: Mosby Year Book.

Greenland, P., Reicher-Reiss, H., Goldbourt, U., & Behar, S. (1991). In-hospital and 1-year mortality in 1,524 women after myocardial infarction: Comparison with 4,315 men. Circulation, 83(2), 484-490.

Grundy, S. (1986). Cholesterol and coronary heart disease: A new era. Journal of the American Medical Association, 256(20), 2849-2858.

Grundy, S. M., & Vega, G. L. (1992). Two different views of the relationship of hypertriglyceridemia to coronary heart disease. Archives of Internal Medicine, 152(1), 28-34.

Grundy, S. M., Vega, G. L., & Bilheimer, D. W. (1985). Kinetic mechanisms determining variability in low density lipoprotein levels and rise with age. Arteriosclerosis, 5(6), 623-630.

Guyton, A. (1987). Lipid metabolism. Textbook of medical physiology. Philadelphia: W. B. Saunders.

Hammond, E. G., & Horn, D. (1958). Smoking and death rates--Report on forty-four months of follow-up of 187,783 men: Death rates by cause. Journal of the American Medical Association, 166(11), 1294-1308.

Hartz, A., Grubb, B., Wild, R., VonNort, J. J., Kuhn, E., Freedman, D., & Rimm, A. (1990). The association of waist hip ratio and angiographically determined coronary artery disease. International Journal of Obesity, 14(8), 657-665.

Heiss, G., Johnson, N. J., Reiland, S., Davis, E. E., & Tyroler, H. A. (1980). The epidemiology of plasma high-density lipoprotein cholesterol levels: The Lipid Research Clinics Program Prevalence Study: Summary. Circulation, 62(Suppl. 4), 116-136.

Heller, R. F., & Jacobs, H. S. (1978). Coronary heart disease in relation to age, sex, and the menopause. British Medical Journal, 1, 472-474.

Heyden, S., Heiss, G., & Bartel, A. G. (1980). Sex differences in coronary mortality among diabetics in Evans County, Georgia. Journal of Chronic Disease, 33(3), 265-273.

Higginbotham, M. B., Morris K. G., Coleman, R. E., & Cobb, F. R. (1984). Sex-related differences in the normal cardiac response to upright exercise. Circulation, 70(3), 357-366.

Hjermann, I. (1985). Primary prevention of coronary heart disease [Editorial]. Acta Medica Scandinavica, 218(2), 1-4.

Holmes, D. R., Elveback, L. R., Frye, R. L., Kottke, B. A., & Effefson, R. D. (1981). Association of risk factor variables and coronary artery disease documented by angiography. Circulation, 63(2), 293-299.

Hosaki, S., Kishimoto, T., Yamauchi, M., & Shiina, S. (1985). Serum lipoproteins in a Japanese rural community with low cardiovascular mortality. Atherosclerosis, 54(1), 43-47.

Hubert, H. B., Feinleib, M., McNamara, P. M., & Castelli, W. P. (1983). Obesity as an independent risk factor for cardiovascular disease: A twenty-six year follow-up of Framingham Heart Study participants. Circulation, 67(5), 968-77.

Hulley, S. B., Rosenman, R. H., Bawol, R. D., & Brand, R. J. (1980). Epidemiology as a guide to clinical decisions: The association between triglyceride and coronary heart disease. New England Journal of Medicine, 302(25), 1383-1389.

Jackson, R. L., Morrisett, J. D., & Gotto, A. M., Jr. (1976). Lipoprotein structure and metabolism. Physiological Reviews, 56(2), 259-316.

Jacobs, D. R., Mebane, I. L., Bangdiwala, S. I., Criqui, M. H., & Tyroler, H. A. (1990). High density lipoprotein cholesterol as a predictor of cardiovascular disease mortality in men and women: The follow-up study of the Lipid Research Clinics Prevalence Study. American Journal of Epidemiology, 131 (1), 32-41.

Johansson, S., Bondjers, G., Fager, G., Wedel, H., Tsipogianni, A., Olafsson, S., Vedin, A., Wiklund, O., & Wilhelmsson, C. (1988). Serum lipids and apolipoprotein levels in women with acute myocardial infarction. Arteriosclerosis, 8(6), 742-749.

Kannel, W. B. (1981). Update on the role of cigarette smoking in coronary artery disease. American Heart Journal, 101(3), 319-328.

Kannel, W. B., Castelli, W. P., & Gordon, T. (1979). Cholesterol in the prediction of atherosclerotic disease: New perspectives based on the Framingham Study. Annals of Internal Medicine, 90(1), 85-91.

Kannel, W. B., Castelli, W. P., Gordon, T., & McNamara, P. M. (1971). Serum cholesterol, lipoproteins, and risk of coronary heart disease: The Framingham Study. Annals of Internal Medicine, 74(1), 1-12.

Kannel, W. B., & McGee, D. L. (1979). Diabetes and glucose tolerance as risk factors for cardiovascular disease: The Framingham Study. Diabetes Care, 2(2), 120-126.

Kannel, W. B., McGee, D. L., & Castelli, W. P. (1984). Latest perspective on cigarette smoking and cardiovascular disease: The Framingham Study. Journal of Cardiac Rehabilitation, 4(7), 267-277.

Kannel, W. B., McGee, D., & Gordon, T. (1976). A general cardiovascular risk profile: The Framingham Study. American Journal of Cardiology, 38(2), 46-51.

Kannel, W. B., Sorlie, P., & McNamara, P. M. (1979). Prognosis after initial myocardial infarction: The Framingham Study. American Journal of Cardiology, 44(1), 53-59.

Kesteloot, H., Huang, D. X., Yang, X. S., Claes, J., Roseneau, M., Goboers, J., & Joosens, J. V. (1985). Serum lipids in the People's Republic of China: Comparison of Western and Eastern populations. Arteriosclerosis, 5(5), 427-433.

Knoke, J. D. & Hawkins, D. L. (1985). Estimating baseline values of the variables of intervention in a clinical trial. Controlled Clinical Trials, 6(2), 136-145.

Knuiman, J. T., West, C. E., Katan, M. B., & Hautvast, J. G. (1987). Total cholesterol and high density lipoprotein cholesterol levels in populations differing in fat and carbohydrate intake. Arteriosclerosis, 7(6), 612-619.

Lapidus, L., Bengtsson, C., Larsson, B., Pennert, K., Rybo, E., & Sjostrom, L. (1984). Distribution of adipose tissue and risk of cardiovascular disease and death: A 12 year follow up of participants in the population study of women in Gothenburg, Sweden. British Medical Journal, 289, 1257-1261.

Larsson, B., Bjorntorp, P., & Tibblin, G. (1981). The health consequences of moderate obesity. International Journal of Obesity, 5(2), 97-116.

Larsson, B., Svardsudd, K., Welin, L., Wilhelmsen, L., Bjorntorop, P., & Tibblin, G. (1984). Abdominal adipose tissue distribution, obesity, and risk of cardiovascular disease and death: 13 year follow up of participants in the study of men born in 1913. British Medical Journal, 288, 1401-1404.

Leaf, D. A. (1988). A woman's heart. An update of coronary artery disease risk in women. Western Journal of Medicine, 149(6), 751-757.

Leaf, D. A. (1990). Women and coronary artery disease: Gender confers no immunity. Postgraduate Medicine, 87(7), 55-60.

Leaverton, P. E., Sorlie, P. D., Kleinman, J. C., Dannenberg, A. L., Ingster-Moore, L., Kannel, W. B., & Cornoni-Huntley, J. C. (1987). Representativeness of the Framingham risk model for coronary heart disease mortality: A comparison with a national cohort study. Journal of Chronic Disease, 40(8), 775-784.

Lipid Research Clinics Coronary Primary Prevention Trial Results I [Lipid Research Clinics Program I]. (1984). Reduction in incidence of coronary heart disease. Journal of the American Medical Association, 251(3), 351-362.

Lipid Research Clinics Coronary Primary Prevention Trial Results II [Lipid Research Clinics Program II]. (1984). The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. Journal of the American Medical Association, 251(3), 365-371.

Mancia, G. (1988). Opening remarks: The need tc manage risk factors of coronary heart disease. American Heart Journal, 115(1), 240-241.

Mancia, G., Groppelli, A., Casadei, R., Omboni, S., Mutti, E., & Parati, G. (1990). Cardiovascular effects of smoking. Clinical and Experimental Hypertension-Part A: Theory and Practice, A12(5), 917-929.

Manninen, V., Elo, M. O., Frick, M. H., Haapa, K., Heinonen, O. P., Heinsalmi, P., Helo, P., & Huttunen, J. K., Kaitaniemi, P., Koskinen, P., Maenpaa, H., Malkonen, M., Manttari, M., Norola, S., Pasternack, A., Pikkarainen, J., Rono, M., Sjoblom, T., & Nikkila, E. A. (1988). Lipid alterations and decline in the incidence of coronary heart disease in the Helsinke Heart Study. Journal of the American Medical Association, 260(5), 641-651.

Manninen, V., Tenkanen, L., Koskinen, P., Huttunen, J. K., Manttari, M., Heinonen, O. P., & Frick, M. H. (1992). Joint effects of serum triglyceride and LDL cholesterol and HDL cholesterol concentrations on coronary heart disease risk in the Helsinki Heart Study. Circulation, 85(1), 37-45.

Marti, B., Tuomilehto, J., Salomaa, V., Kartovaara, L., Korhonen, H. J., & Pietinen, P. (1990). Body fat distribution in the Finnish population: Environmental determinants and predictive power for cardiovascular risk factor levels. Journal of Epidemiology in Community Health, 45(2), 131-137.

McGill, H. C. (1988). The cardiovascular pathology of smoking. American Heart Journal, 115(1), 250-256.

Meade, T. W., Mellows, S., Brozovic, M., Miller, G. J., Chakrabarti, R. R., North, W. R. S., Haines, A. P., Stirling, Y., Imeson, J. D., & Thompson, S. G. (1986). Haemostatic function and ischemic heart disease: Principal results of the Northwick Park Heart Study. Lancet, 2, 533-537.

Memmer, M. K. (1989). Hypercholesterolemia: Causes, significance, and diagnosis. Progress in Cardiovascular Nursing, 4(2), 33-39.

Memmer, M. K. (1989). Hypercholesterolemia: Prevention and control. Progress in Cardiovascular Nursing, 4(2), 40-48.

Miller, G. J., & Miller, N. E. (1975). Plasma-high-density-lipoprotein concentration and development of ischaemic heart-disease. Lancet, 1, 16-19.

Miller, N. E., Thelle, D. S., Forde, O. H., & Mjos, O. D. (1977). The Tromso heart-study: High-density lipoprotein and coronary heart disease: A prospective case-control study. Lancet, 1, 965-968.

Mjos, O. D. (1988). Lipid effects of smoking. American Heart Journal, 115(1), 272-275.

Mock, M. B., Ringqvist, I., Fisher, L. D., Davis, K. B., Chaitman, B. R., Kouchoukos, N. T., Kaiser, G. C., Alderman, E., Ryan, T. J., Russell, R. O., Mullin, S., Fray, D., & Killip, T. (1982). Survival of medically treated patients in the coronary artery surgery study (CASS) registry. Circulation, 66(3), 562-568.

Murdaugh, C. (1990). Coronary artery disease in women. Journal of Cardiovascular Nursing, 4(4), 35-50.

National Heart, Lung, and Blood Institute (NHLBI). (1989). Facts About Blood Cholesterol. Bethesda, MD: Author.

O'Connor, N. T. J., Cederholm-Williams, S., Copper, S., & Cotter, L. (1984). Hypercoagulability and coronary artery disease. British Heart Journal, 52(6), 614-616.

Palmer, J. R., Rosenberg, L., & Shapiro, S. (1989). "Low yield" cigarettes and the risk of nonfatal myocardial infarction in women. New England Journal of Medicine, 320(24), 1569-1573.

Patterson, D. & Slack, J. (1972). Lipid abnormalities in male and female survivors of myocardial infarction and their first degree relatives. Lancet, 1, 393-399.

Pearson, T. A., Bulkley, B. H., Achuff, S. C., Kwiterovich, P. O., & Gordis, L. (1979). The association of low levels of HDL cholesterol and angiographically defined coronary artery disease. American Journal of Epidemiology, 109(3), 285-295.

Pooling Project Research Group: Relationship of blood pressure, serum cholesterol, smoking habit, relative weight and ECG abnormalities to incidence of major coronary events: Final report of the Pooling Project. (1978). Journal of Chronic Diseases, 31(4), 201-306.

Proudfit, W. L., Shirey, E. K. G., & Sones, F. M. (1966). Selective cine coronary arteriography: Correlation with clinical findings in 1000 patients. Circulation, 33(6), 901-910.

Puletti, M., Sunseri, L., Curione, M., Erba, S. M., Borgia, C. (1984). Acute myocardial infarction: Sex-related differences in prognosis. American Heart Journal, 108(1), 63-66.

Reardon, M. F., Nestel, P. J., Craig, J. H., & Harper, R. W. (1985). Lipoprotein predictors of the severity of coronary artery disease in men and women. Circulation, 71(5), 881-888.

Renaud, S., Blache, D., Dumont, E., Thevenon, C., & Wissendanger, T. (1984). Platelet function after cigarette smoking in relation to nicotine and carbon monoxide. Clinical Pharmacology and Therapeutics, 36(3), 389-395.

Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults [Report of the Expert Panel]. (1988). Archives of Internal Medicine, 148(1), 36-69.

Robertson, D., Tseng, C., & Appalsamy, M. (1988). Smoking and mechanisms of cardiovascular control. American Heart Journal, 115(1), 258-261.

Rose, G. A., Blackburn, H., Gillum, R. F., & Prineas, R. J. (1982). Cardiovascular survey methods (2nd ed.). Geneva: World Health Organization

Rosenberg, L., Kaufman, D. W., Helmrich, S. P., Miller, D. R., Stolley, P. D., & Shapiro, S. (1985a). Myocardial infarction and cigarette smoking in women younger than 50 years of age. Journal of the American Medical Association, 253(20), 2965-2969.

Rosenberg, L., Kaufman, D. W., Helmrich, S. P., & Shapiro, S. (1985b). The risk of myocardial infarction after quitting smoking in men under 55 years of age. New England Journal of Medicine, 313(24), 1511-1514.

Rosenberg, L., Palmer, J. R., Shapiro, S. (1990). Decline in the risk of myocardial infarction among women who stop smoking. New England Journal of Medicine, 322(4), 213-217.

Sacks, F. M., Ornish, D., Rosner, B., McLanahan, S., Castelli, W. P., & Kass, E. H. (1985). Plasma lipoprotein levels in vegetarians: The effects of ingestion of fats from dairy products. Journal of the American Medical Association, 254(10), 1337-1341.

Schaefer, E. J., & Levy, P. I. (1985). Pathogenesis and management of lipoprotein disorders. New England Journal of Medicine, 312(20), 1300-1310.

Schatzkin, A., Cupples, L. A., Huren, T., Morelock, S., Mucatee, M., & Kannel, W. B. (1984). The epidemiology of sudden unexpected death: Risk factors for men and women in the Framingham Heart Study. American Heart Journal, 107(6), 1300-1305.

Schoenenberger, J. C. (1982). Smoking change in relation to changes in blood pressure, weight, and cholesterol. Preventative Medicine, 11(4), 441-453.

Selby, J. V., Newman, B., Quesenberry, C. P., Fabsitz, R. R., Carmelli, D., Meaney, F. J., & Slemenda, C. (1990). Genetic and behavioral influences on body fat distribution. International Journal of Obesity, 14(7), 593-602.

Simons, L. A. (1986). Interrelations of lipids and lipoproteins with coronary artery disease mortality in 19 countries. American Journal of Cardiology, 57, 56-106.

Stamler, J., Wentworth, D., & Neaton, J. D. (1986). Is the relation between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? Journal of the American Medical Association, 256(20), 2823-2828.

Strong, J. P., Solberg, L. A., & Restrepo, C. (1968). Atherosclerosis in persons with coronary heart disease. Laboratory Investigation, 18(5), 527-537.

Tachmnes, L., Fernandez, R. J., & Sachner, M. A. (1978). Haemodynamic effects of smoking cigarettes of high and low nicotine content. Chest, 74(3), 243-246.

Talbert, R. L. (1989). Hyperlipidemia. In J. T. DiPiro, R. L. Talbert, P. E. Hayes, G. C. Yee, & L. M. Posey (Eds.), Pharmacotherapy - A pathophysiologic approach (pp. 300-323). New York: Elsevier.

Thom, T. J. (1987). Cardiovascular disease mortality among United States women. In E. D. Eaker, B. Packard, N. K. Wenger, T. B. Clarkson, & H. A. Tyroler (Eds.), Coronary heart disease in women: Proceedings of an N.I.H. workshop (pp. 33-41). New York: Haymarket Doyma.

Tracy, R. E. (1966). Sex difference in coronary disease: Two opposing views. Journal of Chronic Disease, 19, 1245-1251.

Wenger, N. K. (1985). Coronary disease in women. Annual Review of Medicine, 36, 285-294.

Wenger, N. K., & Roberts, R. (1987). Clinical aspects of coronary heart disease in women. In E. D. Eaker, B. Packard, N. K. Wenger, T. B. Clarkson, & H. A. Tyroler (Eds.), Coronary heart disease in women: Proceedings of an N.I.H. workshop (pp. 22-28). New York: Haymarket Doyma.

Wilhelmsen, L. (1988). Coronary heart disease: Epidemiology of smoking and intervention studies of smoking. American Heart Journal, 115(1), 242-249.

Wilhelmsen, L., Berglund, G., Elmfeldt, D., Tibblin, G., Wedel, H., Pennert, K., Vedin, A., Wilhelmsson, C., & Werko, L. (1986). The multifactor primary prevention trial in Goteborg, Sweden. European Heart Journal, 7(4), 279-288.

Willett, W. C., Green, A., Stampfer, M. J., Speizer, F. E., Colditz, G. A., Rosner, B., Monson, R. R., Stason, W., & Hennekens, C. H. (1987). Relative and absolute excess risks of coronary heart disease among women who smoke cigarettes. New England Journal of Medicine, 317(21), 1303-1309.

Wilson, P. W. F., Abbott, R. D., & Castelli, W. P. (1988). High density lipoprotein cholesterol and mortality: The Framingham Heart Study. Arteriosclerosis, 8(6), 737-741.

Wilson, P. W. F., Anderson, K. M., & Castelli, W. P. (1991). The impact of triglycerides on coronary heart disease: The Framingham Study. Atherosclerosis Review, 22, 59-63.

Wong, N. D., Cupples, L. A., Ostfeld, A. M., Levy, D., & Kannel, W. B. (1989). Risk factors for long-term coronary prognosis after initial myocardial infarction: The Framingham Study. American Journal of Epidemiology, 130(3), 469-480.

Zwiauer, K., Widhalm, K., & Kerbl, B. (1990). Relationship between body fat distribution and blood lipids in obese adolescents. International Journal of Obesity, 14, 271-277.

BIOGRAPHICAL SKETCH

Linda R. Beson received her Bachelor of Science in Nursing degree from the College of Mount Saint Joseph in Cincinnati, Ohio, in May, 1975. In 1980, she was commissioned as a captain in the United States Army. During her initial assignment at Moncrief Army Hospital, Fort Jackson, South Carolina, she was selected to attend the Nurse Practitioner/Adult Medical-Surgical Health Care course conducted at Silas B. Hayes Army Hospital, Fort Ord, California. She completed the program in December, 1983, as the honor graduate and was certified by the American Nurses' Association as an adult nurse practitioner in 1985. She separated from the Army in 1985 and was commissioned in the United States Air Force in 1986.

Linda has worked in the fields of medical/surgical nursing, critical care, outpatient adult care, and post-anesthesia care. She is a member of Sigma Theta Tau, Alpha Theta Chapter and is currently a major in the United States Air Force.